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PANEL DISCUSSION ON THE CLINICAL MANAGEMENT OF DISEASES OF THE COLON*

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MODERATOR Z. T. BERCOVITZ: Many aspects of diseases of the colon could be discussed profitably. We have agreed, however, to limit ourselves to diseases of a physical nature. We shall not consider the psychosomatic and emotional elements even though we realize that they are of great importance.

Among the various symptoms are diarrhea, constipation, abdominal cramps, pain, blood, mucus, and loss of weight—a clinical picture with which you all are familiar.

We shall not discuss the complete differential diagnosis, because we assume that everyone is familiar with the various types of diseases of the colon that we shall be discussing and has adequate facilities for making differential diagnostic studies.

A few conditions outside the colon can cause symptoms. For instance, atrophic or hypertrophic gastritis, gastric or duodenal ulcer, and postbulbar duodenal spasm may be the cause of diarrhea or a change in bowel function. Pancreatic disease must always be considered when a patient has some kind of dysfunction of the bowel. Small-bowel malabsorption syndromes, ileitis, diffuse multiple polyposis of the small intestine, carcinoma of the colon, amebic and bacillary dysentery, and amebic granuloma are important in the differential diagnosis. So-called "spastic colitis" is more frequently associated with postbulbar duodenal spasm than with anything else.

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We plan to limit our discussion to 3 or 4 major subjects, namely, carcinoma of the colon, diverticulitis, intestinal obstruction, and ulcerative colitis. We shall start with the question of ulcerative colitis. Dr. Localio, will you take that?

DR. S. ARTHUR LOCALIO: This is one of a number of prepared questions that I shall ask Dr. Bercovitz.

Dr. Bercovitz, *what is the incidence of ulcerative colitis in patients in the older age group?*

MODERATOR BERCOVITZ: Ulcerative colitis can begin after the age of 50 years. We have records of people who were entirely well until that time and then had an attack of ulcerative colitis of the acute fulminating type. Among 30 patients over the age of 50 years recently studied, in 11 the colitis developed after they had passed that mark.

DR. LOCALIO: Dr. Bercovitz, *in what form does ulcerative colitis occur in patients in the older age group?*

MODERATOR BERCOVITZ: There are 2 forms of ulcerative colitis. I am accustomed to seeing both.

First is the so-called acute fulminating type. In elderly patients the disease is truly an acutely fulminating one, usually of violent and sudden onset. The patients claim, and I think rightly, that they have not been ill previously or have had only slight bowel irregularity from time to time. They usually give an exact date when the colitis started. Blood, mucus and pus appear in the stool, associated with straining tenesmus and lack of control of bowel movements. The patients find that they cannot reach the bathroom in time, from a distance of 3 or 4 feet. The loss of strength, the weakness and the enervation are severe. The abdomen is swollen and tender. Upon examining these patients, one is impressed with the fact that there is an acute abdominal condition. They have a temperature of 104°–105°F., and they have chills. The large bowel usually can be outlined. The roentgenogram is unusual. Instead of the small contracted bowel that most of us expect in chronic ulcerative colitis, the roentgenogram will show that the bowel is dilated, relaxed and flabby. Later, at operation, one sees the reason for it—the disease has progressed through all the layers of the bowel, and there is no mucosa left. This is truly an acute form of colitis, and many patients last for less than a year. However, the disease may resolve spontaneously. This occurred in 1 patient of a group of 6 observed by us. In this instance, the ulcerative colitis affected only the sigmoid portion of the bowel. The other 5 patients eventually had to be treated surgically.

The second classification is disease that has lasted for a long time. The patients are chronically ill. We have records of patients who have had the disease for as long as forty years. I have been seeing some of them for more than twenty years.

DR. LOCALIO: Dr. Bercovitz, *will you discuss briefly the therapy for the acute fulminating disease in patients of the older age group?*

MODERATOR BERCOVITZ: Therapy of acutely fulminating ulcerative colitis in the older age group presents some serious and difficult problems, because the strength of these patients has been severely depleted. They become dehydrated

so rapidly that we have to be energetic in our approach. We cannot use halfway measures in dealing with this type of disease.

Supportive therapy is the prime requisite. It is usually accomplished by multiple blood transfusions. I use blood freely, taking the calculated risk that eventually the patient may have homologous serum hepatitis. The patient's life is endangered if blood is not used.

The next step is the use of infusions, being careful to balance the electrolytes and to see that the patient receives enough potassium, sodium and chloride. This requires making daily determinations of electrolytes and of proteins. It may be necessary to add serum albumin to the infusions.

The use of antibiotics is important in these patients. In my experience over the past nine years, chloramphenicol (Chloromycetin) has been the drug of choice. In patients with the acutely fulminating form of the disease it is given intravenously in a dosage of 2 or 3 Gm. per day, added to a slow-drip infusion of about 1000 cc. of 10 per cent glucose in distilled water.

In the use of steroids, one must be extremely careful and remember that the adrenocortical reserves of older patients are also depleted. I use small amounts of prednisolone (Meticortelone)—up to 10 mg. once a day. During the acute phase, I have administered as much as 10 mg. of prednisolone twice a day (at breakfast and at lunch time), and as much as 20 mg. of ACTH daily for two or three days, or 10 mg. for four or five days, or 20 mg. three times a week. I am cautious in the use of steroids. I have seen so many accidents, perforations, and serious consequences from the use of steroids that I am certain that they must not be used promiscuously.

A procedure that has recently come into use is the instillation of Meticortelone acetate into the rectum. One cubic centimeter of an aqueous suspension containing 25 mg. of Meticortelone acetate is added to 60 cc. of tepid tap water. The drug thus prepared is instilled through a very fine catheter into the rectum once a day as a retention enema. This is helpful in reducing straining, tenesmus and rectal pain.

The major problem arises in determining when to operate. I should like to ask Dr. Cave to discuss *the indications for surgery in patients with acutely fulminating ulcerative colitis.*

DR. HENRY W. CAVE: Except in cases of impending perforation, massive hemorrhage, multiple skin infections, crippling joint symptoms, continued anemia, and loss of weight and strength, surgical measures should be delayed until 2 factors have been evaluated: 1) the results of conservative management, and 2) the degree of permanent damage to the colon. Needless to say, before any patient is subjected to the risk of surgical interference, meticulous study and treatment should be carried out over a reasonable period. The diet must be carefully adjusted and deficiency states combatted. If predominantly pathologic bacteria are recovered in cultures, specific therapy should be given.

I should like to speak about the acute fulminating type of the disease. We have had a few risky cases. It used to be extremely difficult to know when one

could operate on these patients. At first, we performed ileostomy, then ileostomy and subtotal colectomy, and later total colectomy, the entire surgical procedure being carried out at one time. At present, however, in the acute fulminating stage, there is justification for suggesting subtotal colectomy. Of about 500 patients we have seen with this disease, we have operated on 120; therefore, we have had experience.

MODERATOR BERCOVITZ: Dr. Localio, *will you give us your experience in the surgical treatment of acutely fulminating cases?*

DR. LOCALIO: Our point of view is perhaps slightly more radical than that of Dr. Cave. We favor, and I have performed, total colectomy in one stage. That includes ileostomy and abdominoperineal resection of the rectum. We have had some experience with patients in the older age group with the acute fulminating form and have treated them in the same manner. Any patient with an acute fulminating disease, whether he be old or young, is seriously sick. Therefore, it has been necessary, in order to perform surgery to the extent desired in one stage, to employ aids in addition to those ordinarily available. We favor hypothermic technics during the course of the operative procedure. The anesthesia department at the University hospital is interested in this type of anesthetic technic for the seriously sick patient; they have gained considerable experience and have been of a great deal of assistance to us. By decreasing the metabolic need through lowering body temperature to 31° to 32°C., the patient withstands the operative procedure with more ease. This is particularly true of the patient who is seriously ill due to peritonitis, either from a free perforation or secondary to transgression of bacteria through the gut wall that has become so devitalized by huge ulcerations that it is no longer a barrier to bacterial movement.

Operating in this manner, the surgeon can proceed with fair rapidity. The patient's blood pressure usually is considerably lower than it would be under conventional methods of management. Blood loss is diminished. Relaxation is satisfactory, with amounts of anesthetic agent less than normal. Oxygenation of tissues is excellent. We think that with such help one can carry the critically-ill patient through the operation with greater safety than was possible formerly.

MODERATOR BERCOVITZ: We have decided that, for the operation, we must have a medical and surgical team working together. I am going to take the liberty of injecting a few points here to indicate that by working together we can do much to make possible this type of radical surgery.

Preliminary preparation of the patient with adequate blood transfusions, with adequate amounts of protein, and with Chloromycetin intravenously in a dosage of 2 or 3 Gm. per day, has proved to be a most efficient method of sterilization of the bowel. Thus, even though the surgeon may find the bowel so degenerated that he can hardly handle it, and soiling of the peritoneal cavity with bowel contents inevitable, there is no problem of secondary peritonitis caused by the soiling.

The addition of adequate amounts of electrolytes and protein to the infusions is also important. A common mistake is to give infusions without adequate proteins. I have seen patients become water logged as a result of constant pouring in of 2500 to 3500 cc. of water without enough blood and protein. Repeated

blood transfusions are required in amounts of 1000 or 1500 cc. in order to maintain the blood level (hematocrit) at a level suitable for the needs of the patient.

It is during the immediate postoperative period that steroids are of the greatest value. Cortisone intravenously is effective in maintaining patients during the critical postoperative period, but its administration must be carried on under careful observation. Not infrequently, we find it necessary to give 100 mg. in one of the infusions during the operation, and then, on the first day, 100 mg. by intramuscular injection or by infusion followed by a slight decrease in dosage as the indications become less acute and as the patient's blood pressure is maintained. The dosage probably can be reduced to 75 mg. the next day, or perhaps 50 mg., and thereafter reduced further. Minute doses of ACTH may be added for the stimulating effect—20 units once a day or every other day as needed. All of this is in co-operation with the surgeon.

DR. LOCALIO: Dr. Bercovitz, *will you say a few words about the therapy of a patient in the older age group with chronic ulcerative colitis?*

MODERATOR BERCOVITZ: The patient in the older age group with chronic ulcerative colitis is one who needs to be handled very carefully. Most of the principles that I have outlined for the acutely fulminating disease apply here. The only difference is that, as a rule, it is not necessary to use so many infusions. Blood transfusions are not required unless the patient has an episode of bleeding. The question of diet is important. These patients must be watched carefully.

I also use antibiotics, but give them orally. Chloromycetin is usually the best antibiotic and is given in a dosage of 2 Gm. per day. The blood count is carefully watched. Monthly blood counts have been made in 70 patients over a five-year period without observing any changes.

As for steroids, the statements that I made previously apply.

The question of anticholinergic agents always arises. I should like to call your attention to the fact that anticholinergic drugs, as we know them today, act upon the small bowel and reduce the amount of discharge into the large bowel. So far, I have not been able to convince myself that even large doses of any of the anticholinergic drugs (whether Pro-Banthine, Prantal, or some of the newer ones) have much, if any, action upon the large bowel.

It is not necessary to use opium in any of these patients. In the presence of serious pain, phenobarbital is sometimes indicated in combination with belladonna in tablet form. When pain is extremely severe, I resort to the use of tetraethyl ammonium chloride (Etamon chloride) in 3-cc. amounts intramuscularly, never intravenously. This drug furnishes a good measure of relief.

Remissions can occur. I should like to comment on the matter of *relapses and remissions.* A comparison of the seasons of the year in which the initial attack and the relapses took place, may yield interesting data. For example, one patient that I know had 12 recorded relapses. Eight of them were in the same season of the year. December was the month of onset, and December was the month in which 8 of the 12 relapses occurred.

In some patients the remissions are prolonged. One may even be tempted to think that the disease is cured. For example, in one case with a total duration

of thirty-seven years, there was a prolonged remission for nineteen years. However, after nineteen years during which the patient claimed to be perfectly well, multiple constrictions and dilatations could be seen in the colon.

Another patient had a twelve-year remission and then a relapse. I still have not cured the patient of ulcerative colitis, but I have been fortunate in observing such a long remission.

Dr. Cave, *did you want to add something more as to your method of handling chronic cases of ulcerative colitis?*

DR. CAVE: In the older age group we have taken our time and have been careful in selecting patients for surgery. Dr. Bercovitz has just referred to a remission of twelve years' duration, and then a sudden relapse. The disease is difficult to treat. One sees so many people with the chronic form. They become panicky after a while, and sometimes demand surgery.

In the chronically diseased older patient, the question resolves into whether or not one is going to do something for the patient, and when. I firmly believe that many of these patients wait too long before being turned over to the surgeon. I think that holds true in many instances in which the physician has done the best he could. A remission has occurred, but after a long period of time there has been a relapse. Then the patient comes to the surgeon. I do not say this because I am a surgeon. I think it is a fact that many of these people have resisted surgery too long.

MODERATOR BERCOVITZ: Dr. Cave, *what would be your procedure of choice in these cases?*

DR. CAVE: When first confronted with this disease some twenty-eight years ago, the surgeons at various clinics over the country performed ileostomy or appendicostomy or cecostomy. They found that these would do no good. Then they performed subtotal colectomy with ileostomy. Finally, total colectomy has become the vogue, and I think justly so, as Dr. Localio has said. Without question, one must individualize the care of these patients, but not let them wait too long.

MODERATOR BERCOVITZ: Dr. Cave, *could you give us some indication of the results of surgery?*

DR. CAVE: We have been quite satisfied with our results. Our fatalities have numbered 17 during the past twenty years. In the older age group death occurred in 2 patients with peritonitis and in 1 with massive hemorrhage. Coronary thrombosis of undetermined cause occurred in 1 patient after two weeks of congestive heart failure. Ulcerative colitis is a risky disease no matter in what stage you take it. Up to the present, surgery is the procedure of choice.

MODERATOR BERCOVITZ: Dr. Cave, *what is the incidence of cancer in chronic ulcerative colitis?*

DR. CAVE: Cancer develops in approximately 9 per cent of patients with chronic ulcerative colitis. At the Lahey clinic, Dr. Cattell told me six months ago that the mortality rate was 11 per cent among persons in whom cancer occurred in addition to chronic ulcerative colitis.

MODERATOR BERCOVITZ: Dr. Brunschwig, what has been your experience as to the incidence of cancer in ulcerative colitis?

DR. ALEXANDER BRUNSCHWIG: I cannot give any specific figures, but as Dr. Cave has pointed out, it seems to be greater among that group of patients than among the population at large.

MODERATOR BERCOVITZ: Dr. Localio, what is your experience in that regard?

DR. LOCALIO: I can only reiterate what Dr. Cave and Dr. Brunschwig have said.

MODERATOR BERCOVITZ: Dr. Localio, *what types of obstruction of the large bowel might we expect to find in the older age group?*

DR. LOCALIO: Intestinal obstruction in ulcerative colitis is unusual. The most common cause of obstruction of the large intestine in the older age group is carcinoma. However, patients with diverticulitis also can have intestinal obstruction.

Volvulus of the left side of the large intestine is something that we see from time to time in a place like Bellevue Hospital, where the population is largely from Eastern European countries.

Intestinal obstruction in the elderly patient is frequently a very deceptive disease. The obstruction can be well established before the patient complains of symptoms. Pain is a late symptom, or may not be present at all.

MODERATOR BERCOVITZ: *What about diarrhea in intestinal obstruction,* Dr. Localio?

DR. LOCALIO: An obstructing lesion of the large intestine, particularly on the left side and before the obstruction is complete, is frequently associated with diarrhea as one of the presenting complaints. The patient with carcinoma of the sigmoid colon who has alternating episodes of constipation and diarrhea actually is manifesting early obstructive symptoms.

MODERATOR BERCOVITZ: *What should be done with regard to surgery in the colon in the case of volvulus?*

DR. LOCALIO: Some of the people with volvulus can be treated, as far as the emergency is concerned, by nonoperative means. We have a resident at Bellevue Hospital who will attest to the efficacy of sigmoidoscopy. A sigmoidoscope can be inserted; the rectal tube passed through it derotates the volvulus and a sudden massive expulsion of material occurs. If one can accomplish reduction in this manner, it is fortuitous.

When surgery is required, the operation of choice, if there has been no interference with the blood supply and no gangrene, is derotation of the intestine. The gut is deflated by suction through a large trocar, and definitive therapy is postponed. In cases of late volvulus, when there has been a change in the blood supply and the intestine is gangrenous, some kind of resection is required. Primary anastomosis is hazardous. The old exteriorizing operations, which Dr. Cave and Dr. Brunschwig know far better than I, are indicated in this particular situation.

MODERATOR BERCOVITZ: Dr. Brunschwig, would you like to add anything about the surgical therapy of volvulus? If not, may we turn to the subject of diverticulitis? *What about bleeding in diverticulitis?*

DR. BRUNSCHWIG: The bleeding associated with diverticulitis may vary from that which is negligible from the standpoint of clinical management to that

dominating the whole symptomatology. Massive hemorrhage can occur from a colon in which there is diverticulitis and in which there are diverticula that are not inflamed, or are so mildly inflamed that symptoms do not arise from them. I have in mind a number of patients whom I have seen here and there or whom I have been told about, in whom massive hemorrhages have occurred. Exhaustive diagnostic studies were carried out in these people on more than one occasion. Finally, it was found that they were bleeding from vessels that encircle the diverticula. Dr. Nore, Professor of Surgery at the University of Louisville, and his group have made an ingenious study of specimens of diverticulitis in the colon and have shown that large blood vessels exist around these diverticula. When there is even a small degree of inflammation, these vessels may open and give rise to massive hemorrhage.

We all know of cases of massive hemorrhage from the gastro-intestinal tract, of undetermined origin. Some of these eventually prove to be due to diverticula. I know of 2 instances in which a right colectomy was performed simply on a hunch that this was the cause. In both instances, series of diverticula, not inflamed to the point of producing symptoms, were present. The bleeding came from the vessels around these diverticula. When right colectomy was performed, the hemorrhages stopped.

MODERATOR BERCOVITZ: Dr. Brunschwig, *do I understand from what you say that there can be diverticulosis with hemorrhage without diverticulitis?*

DR. BRUNSCHWIG: Without *clinical* diverticulitis, I would say. It is hard to believe that there can be an escape of blood from absolutely normal or uninflamed diverticula. Sudden and massive hemorrhage, or continued severe hemorrhage, may occur without symptoms suggesting diverticulitis.

MODERATOR BERCOVITZ: Dr. Brunschwig, *what would you do if you had a patient like that—sudden massive hemorrhage, no previous radiographic examination, and no history of diverticulitis antedating this experience?*

DR. BRUNSCHWIG: One would have to study the situation carefully to determine the source of bleeding. Any number of lesions could be the source of massive hemorrhage, but if the results of studies of the upper gastro-intestinal tract are repeatedly negative and the quality of blood suggests an origin low in the gastro-intestinal tract, a careful search should be made for the presence of diverticula.

MODERATOR BERCOVITZ: *Should a barium enema be used in these patients in case of bleeding?*

DR. BRUNSCHWIG: I would treat the bleeding conservatively with bed rest, replacement of blood, suppression of stools, and medical means insofar as possible. I do not believe that a barium enema should be used immediately to try to find diverticula in the face of massive bleeding.

MODERATOR BERCOVITZ: *What is the relation between diverticulitis and carcinoma? In other words, does the presence of diverticula in the large bowel favor the development of carcinoma?*

DR. BRUNSCHWIG: I know of no statistics to indicate, that carcinoma occurs more frequently in colons that are the site of symptom-producing diverticula.

I am sure we all have seen cases in which diverticula and carcinoma of the colon coexist. Making the diagnosis of diverticulitis should not put the clinician completely at rest, thinking he has covered the whole situation. If there is a suspicion of carcinoma, both conditions may be present.

MODERATOR BERCOVITZ: Dr. Localio, *will you discuss the indications for surgery in diverticulitis or diverticula with or without hemorrhage?*

DR. LOCALIO: There are not many indications for surgery in diverticulosis. We have seen 2 patients who required emergency colectomy for bleeding of diverticula, probably with some diverticulitis that was not discernible clinically. Massive bleeding was of such extent that the colon had to be resected in order to save life.

The indications for surgery in diverticulitis are in the process of being changed radically. Many gastroenterologists will disagree with the surgeons as to the true indications. When there is perforation of the diverticulum with peritonitis, or when there is obstruction, operation should be performed. There is little argument about that. The argument comes with regard to persons who have repeated episodes of acute diverticulitis with varying radiographic changes and maybe minor perforations. In many sections of the country, surgeons believe that these patients should be operated upon prior to the appearance of sequelae such as intestinal, cutaneous, or vesico-intestinal fistulae. Satisfactory surgical-risk patients who have had numerous episodes of acute diverticulitis, even without major complications, should be operated upon.

MODERATOR BERCOVITZ: Dr. Cave, *do you think that there is any relation between diverticulitis and ulcerative colitis?*

DR. CAVE: I do not think so. They are independent lesions. Some years ago, Dr. Dan Jones of Boston made the statement that diverticula never bled. If the condition was diverticulitis and there was bleeding, it would stop of its own accord. I do not think that there is any relation between them.

I had an interesting time a week ago in Washington talking to some military surgeons. On this panel was Dr. Harvey Stone, a distinguished surgeon from Baltimore. He gave me permission to report the case of a patient of his who had massive bleeding from diverticulitis. He did not know what to do about it, so he discussed it with his best friend. They decided that, if the patient bled once more, they would perform a resection. Dr. Stone stated that he would let a patient bleed once but, if the patient bled again, he would operate and perform a resection.

MODERATOR BERCOVITZ: Dr. Brunschwig, *what type of surgery should be performed in a case of diverticulitis? Did I understand you correctly about hemicolectomy?*

DR. BRUNSCHWIG: It depends upon where the diverticulitis occurs. It is a question of resecting that portion of the intestine which seems to be involved in producing lesions. Diverticula may be present throughout the entire colon, but one would certainly not perform total colectomy simply because of the presence of diverticula. Surgery is indicated only when symptoms are produced, that is, hemorrhage, inflammation, perforation, and obstruction.

MODERATOR BERCOVITZ: Dr. Localio, *is a one-stage procedure suitable for operating on diverticulitis?*

DR. LOCALIO: In some situations, a one-stage operation is very suitable. The chronic obstructing type of diverticulitis is such a situation. However, the patient with a free perforation and peritonitis cannot be handled with a one-stage operation. Such a patient usually requires drainage and some kind of defunctionalizing colostomy. Resection of the diseased colon and closure of the colostomy is performed at a later time.

MODERATOR BERCOVITZ: Dr. Brunschwig, *will you please give us a thumbnail sketch of your thinking with regard to carcinoma of the colon?*

DR. BRUNSCHWIG: Carcinoma of the colon varies tremendously in evolution, as do all carcinomas. Among cases of carcinoma of the colon, there is one group which can be distinguished only by its clinical activities and not by microscopic studies. I am referring to the group in which the carcinoma seems to grow mainly by local extension. If it does metastasize, it metastasizes relatively late.

Clinically, the lesion appears to be "spread around," but actually it may not be as widespread as one at first thinks. This apparent local extension of the disease does not necessarily indicate virulence or rapid growth. It should not discourage excision. If one makes a radical attack upon these lesions that seem to be spreading locally, he will be surprised at the number of salvages. By that, I mean five or more years' survival achieved in the face of a situation that years ago was considered inoperable by virtue of its spread from its site of origin to neighboring structures. I have several cases of persons over 50 years of age who have survived for six to twelve years.

Sometimes, anal colon cancers perforate into the vagina. Even when they do perforate forward one can perform a combination of abdominal perineal hysterectomy, or abdominal perineal resection of the lower colon and hysterectomy, which permits a prolonged survival.

Krukenberg tumors present as large masses, which may be metastases from small colon cancers. They are attacked by radical panhysterectomy, and effective palliation is achieved.

A very radical operation, namely pelvic exenteration, is performed for locally infiltrating cancers in the pelvis. The patients have to wear bags over the wet colostomy, but they adjust to them well.

I cite these examples to illustrate the point that, before anybody says that a given cancer is inoperable or hopeless, and that the patient is through because of the fact that the carcinoma has invaded an adjacent organ, one must consider that patients of this group with locally invading cancers can survive for an indefinite period if the lesion is widely excised.

MODERATOR BERCOVITZ: Dr. Brunschwig, we are greatly impressed and want to thank you for presenting these data to us. We congratulate you on what you have done.

I should like to ask one question. *What about radiation therapy following this type of surgery?*

DR. BRUNSCHWIG: Ordinarily, I do not use radiation therapy when no gross

evidence of the disease remains. However, studies just completed in our hospital (Deddish *et al.*) suggest that cancer of the colon is not as radioresistant as it is generally thought to be, and that, with a combination of radical surgery and irradiation of moderate intensity (that is, not a high dose), the percentage of survivors is greater following the radical operation when pre- and postoperative radiation has been used. I say that to bring out the point that we cannot say that radiation is of no use. I have always considered cancer of the colon to be virtually radioresistant as far as primary treatment is concerned. Whether or not irradiation can add something to save the patient after the growth has been removed, I cannot say. That is something to think about and to learn from future experience. I am convinced that we simply cannot toss it out and say that is of no use.

MODERATOR BERCOVITZ: Dr. Brunschwig, thank you again for your contribution. Now, we shall make available some time for questions from the floor.

DR. NATHANSON (Brooklyn): I should like to ask 2 specific questions. *In the care of the patient with ulcerative colitis and massive hemorrhage, do you rely upon blood transfusions alone, or do you use other methods in an attempt to control bleeding? Have you ever instilled an astringent mixture into the colon?*

Dr. Bercovitz mentioned the diet. *Could you be a little more specific as to the diet?*

MODERATOR BERCOVITZ: In answer to your question about the use of astringents by rectal instillation—over a period of years we have used many different kinds of medications designed to accomplish just what you have in mind. We have discarded them one by one, and at present we are using few rectal medications. We have used almost everything imaginable in an effort to decrease the amount of bleeding. Blood transfusion still is our method of choice. We try to replace blood as fast as it is being lost, and to keep ahead of the loss. Intrarectal medication has failed us. In the earlier days, as Dr. Cave mentioned, cecostomies were performed. We even went so far as to use the cecostomy as a means for the instillation of various medications such as zinc, aluminum preparations, silver, permanganate, and cod liver oil. I used to think that cod liver oil had some value, but I did not continue it because the patients did not seem to improve.

The recent experience with Meticortelone acetate instilled into the rectum is interesting and worth while, but I have not been using it long enough to make a statement. Does than answer your question?

DR. NATHANSON: *What about estrogens?*

MODERATOR BERCOVITZ: I have not used them to any great extent but I know that they are being used by some physicians with excellent results. The problem is as simple as this: If one is going to talk about inducing a remission, that is one thing; but if one is going to talk about cure, that is something else, and I have no contributions to make.

With reference to the question of diet, I must confess that I am a bit radical. My diet slips contain one word—food. My plan is to have the patient take all the food he possibly can. A series of studies that I made in 1939, 1940 and 1941 showed a marked decrease in the absorption rate and a marked loss of various

substances. These patients need more food than we do; I cannot see that food hurts them. On the other hand, they feel better and have a sense of freedom. If one considers that most of the bowel movements containing blood, mucus and pus are caused by inflammation, irritation, and spasm of the lower segment of the intestine, he will realize that the more food the patient receives the better he will be.

Are there any other questions?

SPEAKER FROM THE FLOOR: *What diet is used to prevent diverticulitis in a patient with diverticulosis?*

MODERATOR BERCOVITZ: Dr. Localio, would you like to discuss that?

DR. LOCALIO: I am a surgeon and I do not treat patients of that kind medically, but I should think that in diverticulosis there should be some restriction on the amount of residue in the diet. Whether or not this impression be correct, it seems to me that I see more people with acute diverticulitis and with perforated diverticula in the summer when corn and other high-residue foods are available.

SPEAKER FROM THE FLOOR: (To Dr. Localio) *Is there any medical treatment for diverticulitis before surgery is undertaken? Medical treatment has not been mentioned.*

DR. LOCALIO: There certainly is. The majority of patients with diverticulitis should be treated medically, as they represent cases of simple inflammation. The diverticula will quiet down with a low-residue diet. An intestinal bacteriostatic agent that is not absorbed (*e.g.*, Sulfasuxidine) will soften the stool so that it can be passed easily. Support with antibiotics should be given if the temperature is elevated. One waits out these attacks. They subside, and if they do not recur repeatedly, conservative treatment should be continued.

SPEAKER FROM THE FLOOR: (To Dr. Brunschwig) *Was the liver involved in any of your patients who survived?*

DR. BRUNSCHWIG: No. Metastases to the liver indicate an advanced stage. I would not attempt massive resection in the presence of metastases, although a classical localized resection for palliation is indicated to obviate obstruction and to avoid performing a colostomy.

That brings up the possibility of palliative treatment of liver metastases. It sounds so ridiculous that one ought not even think about it. However, we should realize that it is not so long ago that surgeons began removing solitary metastases to the lungs from intra-abdominal cancer. Some of these patients—there are 30 and 40 in the literature—have survived more than five years.

Some metastases to the liver from carcinoma of the colon may be large and produce a great deal of pain. In that particular situation, one should consider palliation by means of resecting the metastases. I know of one case—it is not my own—in which the left lobe of the liver was removed because of massive metastases, six years after a left nephrectomy for hypernephroma. The patient is living six years after the removal of the left hepatic lobe—twelve years after removal of the kidney for hypernephroma. I have removed liver metastases for the purpose of palliation in patients who have survived for a year to two and a half years afterwards. They were satisfied with the palliation they obtained.

SPEAKER FROM THE FLOOR: *You spoke of remission in ulcerative colitis lasting for years. Do you think of any special treatment besides diet that will help?*

MODERATOR BERCOVITZ: Do you mean during the period of remission?

SPEAKER FROM THE FLOOR: Yes.

MODERATOR BERCOVITZ: Our problem through the years has been trying to handle these patients in the period of remission in such a way as to prevent relapse. I must confess that I have tried to feed them. I find that the least amount of medication the better, and the least attention to their disease the better. The more that we can impress upon these patients that they are normal people and that they should go back to their usual mode of life and do the things that they are accustomed to doing, the better off they will be. I have come to the conclusion that there is no certain method of preventing relapses. The continued use of antibiotics is not the answer. The continued use of antispasmodic and anticholinergic agents is not the answer. Morphine and opiates are not the answer. It is best to get these people to live as normal a life as possible and to forget that they have colitis. Then, if it returns, "it is one of those things." We help the patients to adjust to the relapse. All of them are terribly disappointed if they have a relapse after five, ten or nineteen years. They had thought that they were finished with the disease. Again, I want to stress relapse with reference to the season. This is holding true statistically. It helps the patient if he knows that the relapse has occurred during the season when the disease started and when he has had his other relapses (if any). Realization that the relapse is not due to some terrible thing that he has done prevents a guilt complex.

SPEAKER FROM THE FLOOR: Dr. Brunschwig, you advised against exteriorization during the acute bleeding periods. *What do the other panelists think about massive gastro-intestinal bleeding manifested as severe melena or severe rectal bleeding?*

DR. BRUNSCHWIG: First, let me qualify my statements and say that when a patient comes into the hospital with blood pouring from the anus, I would not think of radiographic study at that time. When he has been put to bed and blood replacement carried out, continued melena or a small amount of bleeding from the rectum would not necessarily contraindicate radiography in due time.

MODERATOR BERCOVITZ: Dr. Localio?

DR. LOCALIO: I agree with Dr. Brunschwig.

DR. CAVE: I also agree.

MODERATOR BERCOVITZ: I think that we are all of one mind on this: assuming that the bleeding has been controlled, we are justified in performing radiography.

SPEAKER FROM THE FLOOR: Dr. Bercovitz, *do you use psychotherapy or do you use a psychiatrist in consultation in ulcerative colitis? As for the seasons, the same thing is found in the case of duodenal ulcer, is it not?*

MODERATOR BERCOVITZ: By definition and exclusion at the beginning of this discussion, we said that we were not going to discuss psychiatry. I will answer your question, though, and say that, as far as I am concerned, I still have to refer my first patient to a psychiatrist. These people all have problems. I submit this to you, doctor: If you and I had a constant stomach-ache, were constantly mov-

ing our bowels ten or fifteen times a day, could not reach the bathroom from the desk chair in our office to the private bathroom a few feet away from us without soiling ourselves, were attorneys and had an accident in the judge's chamber or in the courtroom, or were a woman having a tea party and had a sudden urge and lost it on the living room floor—we would be psychoneurotic. As far as I can see, psychotherapy alone has not done anything for these patients. However, I do spend an average of half an hour with every patient at every office visit. I let them talk, but I am not a psychiatrist.

SPEAKER FROM THE FLOOR: In the discussion of ulcerative colitis, nothing as far as I can remember has been said about etiology. I think that this is important, particularly from the seasonal standpoint, as mentioned. It leads one to believe that probably the actual cause of ulcerative colitis, the infection, has come from or has developed in the upper respiratory tract. The approach to prevention should give some attention to that area. We should think of the cause and the prevention and not always of the cure. When the roof is leaking, go to the roof instead of wiping the floor.

MODERATOR BERCOVITZ: Some fine studies on bacteriology were made in years gone by, when Dr. C. Ward McNeal was Professor of Bacteriology at Post-Graduate. We did not have an answer in bacteriology then, and we do not have it even today. I am giving the latest summary. I know of no etiologic agent. Some of us think that it might be a form of virus. A while ago some evidence indicated that lymphogranuloma virus or some offshoot of that family might be related. The fact remains that the viruses of hepatitis and of poliomyelitis are resident in the bowel. What makes these viruses suddenly attack the liver or the central nervous system, or another virus?

We do not know. I am wondering whether the situation might not be similar with regard to the bowel. I am sorry that I cannot answer your question.

SPEAKER FROM THE FLOOR: *In the case of a cardiovascular accident resulting in fecal incontinence, have you any suggestions for management? Would you advise an ileostomy, or do you have any therapy?*

MODERATOR BERCOVITZ: That is a very difficult, practical, and well thought-out question. I do not know all of the answer to it. I have had some experience with rather large doses of anticholinergic agents which are designed primarily to slow down the discharge of ileal contents into the colon and thereby reduce the amount of discharge from the colon. Sometimes we can produce constipation. I know of no one who has performed an ileostomy or a colostomy in such patients. I should like to ask Dr. Localio. The question concerned a surgical procedure for fecal incontinence in a patient with a cardiovascular accident who has paralysis of the rectum.

DR. LOCALIO: I would not perform any operation. The most that one could accomplish would be to move the incontinence from the gluteal region to the abdominal wall. I certainly would not perform an ileostomy.

MODERATOR BERCOVITZ: *Would it not be cleaner and easier to handle the colostomy.*

DR. LOCALIO: I do not know. I still do not think I would do it.

MODERATOR BERCOVITZ: Dr. Brunschwig, what do you think about it?

DR. BRUNSCHWIG: No one can answer that offhand. One would have to see the specific patient and know the conditions under which the condition obtains, how long it has obtained, and whether the patient is going along for a while. In such a matter, one cannot make a rule and apply it to every patient.

Dr. CAVE: I have nothing to add to that, except to say that it is hard to evaluate properly not only the future of the patient but the present as well. It is the most difficult thing we have to do.

MODERATOR BERCOVITZ: Is there another question?

SPEAKER FROM THE FLOOR: (To Dr. Bercovitz) *How would you manage actively bleeding ulcerative colitis complicated by penetrating duodenal ulcer in a patient who is unable to accept any form of milk or milk products?*

MODERATOR BERCOVITZ: I have been faced with precisely that situation on several occasions. Those are difficult questions. I can give only a rough outline of the way in which I have handled these problems. I use anticholinergic drugs to the fullest extent and give them up to, and almost including the point of toxicity, *i.e.*, the patient can urinate but he is almost constantly constipated. For example, using Pro-Banthine as a baseline, 45 mg. four times per day will usually provide sufficient relief of the hyperperistalsis, the ulcer, the spasm and the acidity. One of the other protein foods can be given instead of milk. Ulcerative colitis should be handled as a separate entity and its therapy should not be confused with that of ulcer.

The use of cereals, scraped and chopped meats, proteins, and gelatin furnishes a fine means of adding protein to the diet. In fact, almost any form of meat is of importance from the standpoint of food and also from the standpoint of neutralizing hyperacidity. Blood transfusions should be given repeatedly until the hematocrit reading is normal.

SPEAKER FROM THE FLOOR: (To Dr. Brunschwig) *Has much work been done on the use of radioactive isotopes in the diagnosis of carcinoma of the bowel?*

DR. BRUNSCHWIG: No, not in the diagnosis. The only use that seems to be made of them is in cancer of the colon that has metastasized, producing troublesome ascites. In these cases, radioactive gold or phosphorus can be instilled into the peritoneal cavity. The resulting inflammatory reaction seals off much of the cavity so that ascites does not occur as frequently as before. That is the only use of radioactive isotopes in cancer of the colon that I know of at present.

INCIDENCE OF VARIOUS TYPES OF CARDIOVASCULAR DISEASES BY AGE GROUP IN THE MALE AND IN THE FEMALE*

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I. INTRODUCTION

Cardiovascular diseases consistently cause approximately half of all deaths in the United States each year. Arteriosclerosis and hypertension together account for more than 90 per cent of all of these deaths (1). This paper is concerned primarily with arteriosclerosis and hypertension because of their importance and also because of the pronounced differences in the incidence of these diseases according to age and sex.

In addition to a review of the literature, this paper contains data collected from the files of 3 general hospitals. These original data are added for the purpose of making some contribution to the understanding of the factors involved in the development of cardiovascular disease.

II. ATHEROSCLEROSIS AND CORONARY HEART DISEASE

A. *Incidence According to Age and Sex*

Atherosclerosis is a specific type of arteriosclerosis characterized by an accumulation of amorphous lipid in the intima of the arteries (2). It is by far the most common type, comprising at least 85 per cent of all arteriosclerotic lesions. Atherosclerosis involves all arteries, including the coronary, renal and cerebral vessels. The involvement of the coronary tree is of particular interest here, because of the differences in incidence with respect to age and sex. Coronary artery disease takes a toll almost equal to that of all malignant tumors combined and it is often the first clinical manifestation of the atherosclerotic process appearing relatively early in life (2, 3).

Review of the literature

Many authors have emphasized the difference in incidence of coronary heart disease between males and females. However, considerable disagreement exists as to the actual incidence of this disorder. Several criteria may be used for defining coronary artery disease, including clinical myocardial infarction or angina pectoris, the degree of coronary atherosclerosis present at autopsy, or heart failure and death attributable to coronary disease. The degree of atherosclerosis found at autopsy cannot always be directly related to clinical coronary disease, because the latter depends on many factors (4–6). For example, a thrombus may develop and occlude an artery which is only slightly atherosclerotic, whereas a severely sclerosed vessel may function normally for a long period. An enlarged heart may become ischemic with a blood flow which would be adequate for a normal sized

* Prize-winning manuscript, Schering Award for medical students.

TABLE 1

Incidence of Clinical Coronary Artery Disease According to Sex

Authors & Reference No.	Total Cases	Per Cent Males	Per Cent Females	Male:Female Ratio
Bland & White (9)	200	84	16	5:1
Parkinson & Bedford (10)	83	86	14	7:1
Schwab & Schulze (11)	335	79	21	4:1
Levy & Boas (12)	1228	84	16	4.9:1
Levine & Brown (13)	145	70	30	3:1
Mintz & Katz (14)	500	68.5	31.5	2.2:1
Parkinson & Bedford (15)	187	91	9	9:1
Conner & Holt (16)	287	85	15	7:1
Bean (17)	300	71	30	3:1
White (18)	200	94	4	24:1*
Average				5:1

*Incidence below the age of 40 years—not included in the average.

TABLE 2

Incidence of Autopsy-proven Coronary Artery Disease According to Sex

Authors & Reference No.	Total Cases	Per Cent Males	Per Cent Females	Male:Female Ratio
Zinn & Cosby (19)	700	68	32	3:1*
Clawson (20)	1,215	71	29	2.5:1**
Clawson & Bell (21)	2,829	63	37	1.7:1*
Willius, Smith & Sprague (22)	1,431	75	25	3:1**

* Record of deaths resulting from coronary disease.

** Record of presence of coronary atherosclerosis of moderate to severe grade.

heart (7). A heart may be well nourished in the presence of severe atherosclerosis if the process has progressed slowly enough for adequate collateral circulation to develop (8). Moreover, the incidence of coronary heart disease is difficult to establish, because groups representing an adequate distribution of the population are difficult to obtain.

Tables 1 and 2 record the incidence of clinical coronary artery disease and of autopsy-proven coronary disease with respect to sex, as reported in the literature. Although a large number of papers have appeared on the subject, most of the clinical studies have been on selected small groups of patients in which male-female ratios were mentioned as incidental findings. No attempts were made to obtain representative samples of the total population. The discrepancies between the clinical data and the autopsy data for coronary disease are immediately apparent. Several authors, in reporting the clinically based data for myocardial infarction supported their evidence from the literature of autopsy reports, but they failed to mention that more autopsies were performed on males than on females (12). Careful examination of the original papers reveals that if the male-female ratios are considered according to the number of autopsies performed on

patients of each sex, they are considerably different (20). The corrected ratios are shown in Table 2.

Original data

A review was made of 1321 consecutive case reports of myocardial infarction in which the diagnosis was based on combined clinical and electrocardiographic evidence. These reports included every case of myocardial infarction on record in 2 large general hospitals. All electrocardiograms taken in these hospitals are

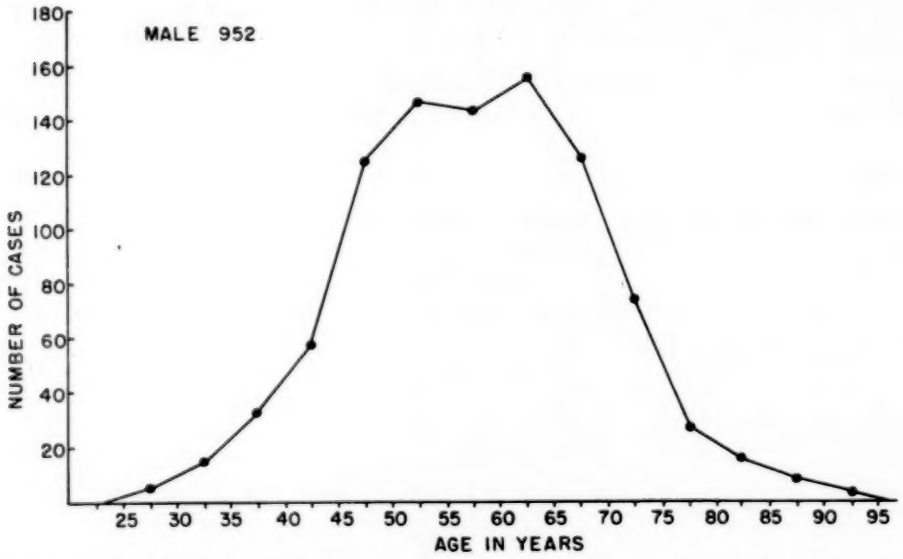

FIG. 1. Incidence of myocardial infarction in males, according to age (952 cases).

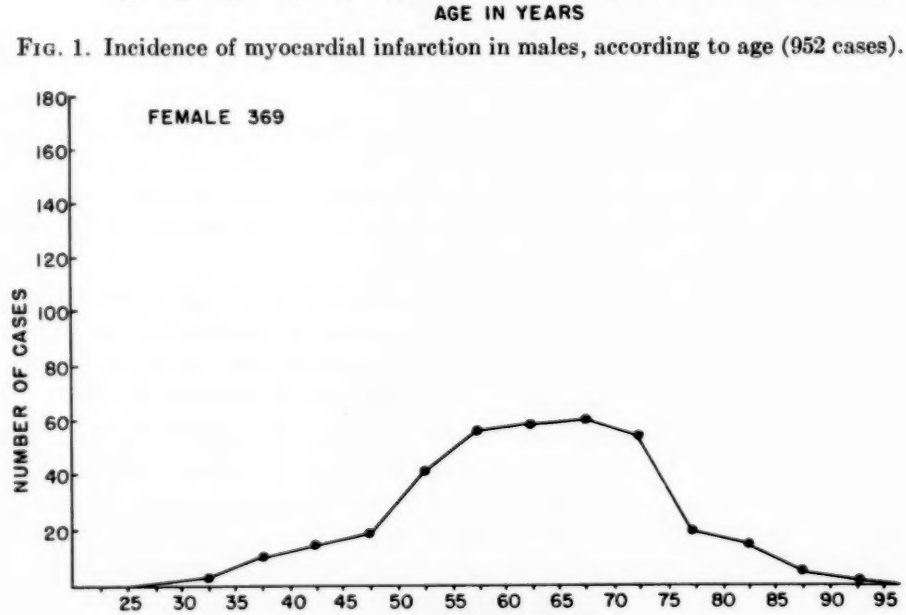

FIG. 2. Incidence of myocardial infarction in females according to age (369 cases).

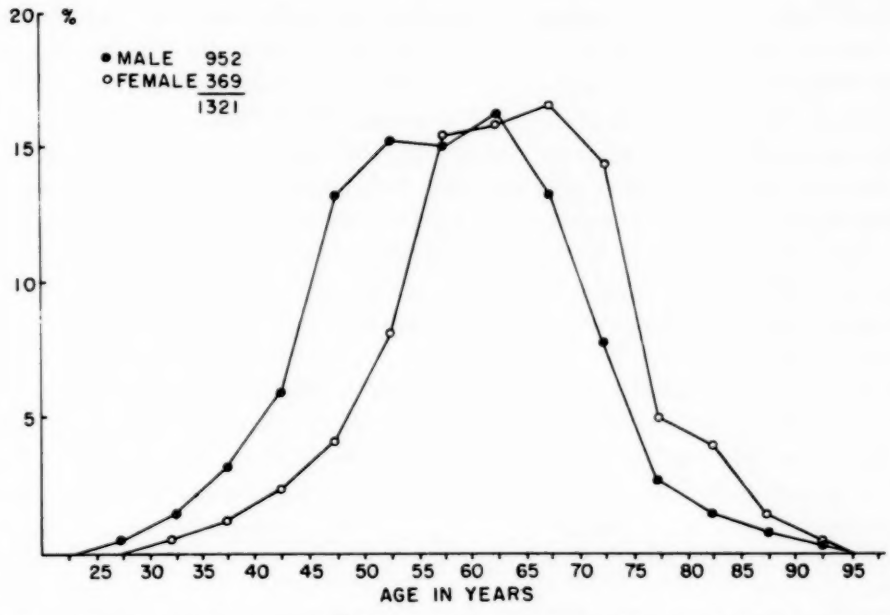

FIG. 3. Age at onset of myocardial infarction in males and in females—on a cumulative percentile basis (1321 cases).

reviewed by a small group of qualified cardiologists, and this fact should imply a relatively high degree of accuracy in the diagnosis of myocardial infarction. The problem involved in estimating the total male-female ratio in the various age groups for the population served by a particular hospital is obvious. The results of this study are based on the assumption of equal male-female ratios. However, the validity of this assumption may be questioned, especially for the older age groups, since females normally outnumber males in the population. Of this relatively large group of 1321 patients, 952 (72 per cent) were males and 369 (28 per cent) were females—yielding a 2.6:1 ratio of males to females. This ratio corresponds with the average for cases of autopsy-proven coronary artery disease. The ratio in this study is considerably lower than the average (5:1) in the previously reported studies on clinical coronary disease. Since our study includes a large number of patients representing all age groups, it possibly provides a more accurate estimate of the incidence than do some of the clinical studies on smaller selected groups.

Figures 1 and 2 show the incidence of myocardial infarction according to age group, in these 1321 cases. Figure 3 demonstrates (on a cumulative percentile basis) the difference in age at onset between males and females. Several observations may be made from these graphs which suggest factors leading to the development of coronary atherosclerosis and occlusion. The incidence of myocardial infarction in males rises sharply rather early in life and reaches a plateau before the age of 55 years. The abrupt fall in the curve of incidence in males after 63 years corresponds somewhat with the decrease in the male population after that age. However, some authors are of the opinion that coronary atherosclerosis

develops less frequently in persons beyond the age of 70 years (23). The incidence of coronary disease in females rises much more slowly until after the age of 45 years, when an abrupt increase occurs; the height of the curve is reached several years after that for males. Gertler, Garn and White (24) reported that when males under 40 years of age were compared with females of the same age group, the sex ratio for myocardial infarction was 24:1. According to the data presented in this paper, the male-female ratio in persons below the age of 40 years is about 6:1, and after 55 years less than 2:1. The disease occurs about equally in both sexes after the age of 65 years. These data suggest that certain factors are either retarding the development of coronary disease in the female or accelerating the process in the male.

One recent report (25) regarding coronary atherosclerosis found at autopsy states that the incidence of atherosclerosis has increased in the female in the past twenty years. The author found that coronary disease in the female even exceeds that in the male for the older age groups since 1940, whereas the reverse is true for the previous years. Further work in necessary to determine whether or not the incidence in females is actually on the increase.

B. *Contributory Factors*

Many factors have been implicated in the development of coronary atherosclerosis, namely, dietary intake of fat, levels of blood lipids, heredity, body build, personality, blood pressure, endocrine imbalance, and associated metabolic diseases. Several of these factors will be considered in order to determine whether or not they explain the difference between the two sexes. The cases of 78 males and 49 females below the age of 55 years with myocardial infarction were carefully reviewed to supplement the literature findings on factors associated with the development of coronary heart disease. These groups were chosen because of the marked difference in incidence of the disease before this age.

Endocrine factors associated with coronary disease

Figure 2 shows an abrupt increase in the incidence of myocardial infarctions in females between 45 and 55 years of age. This sudden change is in contrast to the constant increase of infarction in males beyond the age of 25. Nineteen (39 per cent) of the 49 females below age 55 with coronary disease either had undergone the menopause before age 45 or lacked functioning ovaries because of surgical removal or irradiation. Thirty-four (70 per cent) of the 49 were between the ages of 50 and 55 years, when most women have reached the menopause. These data suggest that coronary disease is rare in the presence of functioning ovaries.

Many authors have suggested that female sex hormones may be important in preventing coronary atherosclerosis, and that after the menopause the female is no longer protected (2, 24, 26). Some evidence even indicates that male sex hormones may accelerate the atherosclerotic process (27). Gertler, Garn and White (24) found that the male with predominant muscularity, compactness and "maleness"—the so-called mesomorphic type—appears to be the most likely candidate for myocardial infarction at an early age.

Experimental evidence supports the concept that female hormones may prevent the development of coronary atherosclerosis. Stamler, Pick and Katz (28) demonstrated that sexually mature chickens exhibit a significant sex difference in susceptibility to cholesterol-induced coronary atherosclerosis. Sexually immature chicks do not show this difference—a fact which supports the suggestion that functioning ovaries may be protective to the female. The same group of investigators (29–34) has reported that estrogen treatment of cholesterol-fed male chicks inhibits coronary atherogenesis. However, aortic atherogenesis proceeds in the usual manner in these animals. Extension seems justified, because there is usually no difference in the incidence of aortic atherosclerosis between young men and young women as in the case of coronary atherosclerosis (2).

Stamler, Pick and Katz (35) reported the results of estrogen therapy in a group of 69 survivors of myocardial infarction under 50 years of age. The patients were divided into placebo-treated and estrogen-treated groups. After two years, in the placebo-treated group there were 6 additional infarctions and 3 fatalities, whereas in the estrogen-treated group there were no additional infarctions and no fatalities. The undesirable effect of estrogens on males has restricted clinical studies of this nature.

The mechanism of this estrogen protection remains unexplained. The influence of female sex hormones on blood lipid levels may partly account for this action, as will be discussed later. However, the effect may be directly on the artery, to prevent deposition or even to mobilize deposited lipid (31).

Serum lipid levels and coronary disease

Considerable evidence suggests a relationship between the levels of blood lipids and the incidence of coronary artery disease. The importance of serum lipoproteins in this relationship has been recently emphasized by Gofman and his associates (26, 36–42). Figure 4 shows a comparison of the average degree of coronary atherosclerosis and the Atherogenic Index of Gofman for the two sexes at various ages (43). The Atherogenic Index is derived from serum lipoprotein values as related statistically to the occurrence of coronary disease. These levels appear to parallel the development of atherosclerosis in both males and females. Low serum lipoprotein levels may partly explain the delayed development of coronary disease in the female. Although several authors question the value of serum lipoprotein determinations in predicting the occurrence of a myocardial infarction, most of them agree that elevated levels are related to an increased incidence of the disease (44–47).

Reports on serum cholesterol values in males and in females have not shown the differences found between the two sexes with respect to serum lipoprotein levels (48–50). These findings suggest that the concentration of serum lipoproteins may be more closely related to the development of coronary atherosclerosis than is the concentration of serum cholesterol. Numerous reports indicate that it is possible to lower serum lipoprotein levels in patients with coronary disease by the administration of female sex hormones (27, 51–55). The authors of these

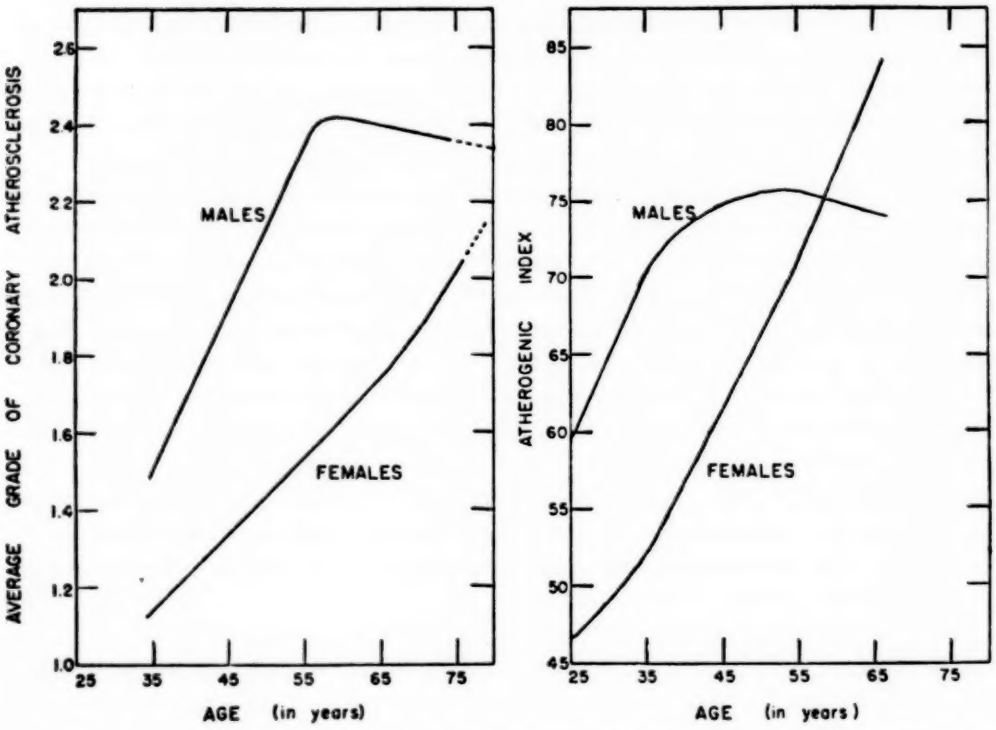

FIG. 4. Comparison of the average grade of coronary atherosclerosis and the Atherogenic Index of Gofman for the two sexes at various ages. (Reproduced with permission from Gofman *et al.*: Index of coronary artery atherogenesis, *Mod. Med.* **21**: 119, 1953.)

publications suggest that this effect may partially explain the relative immunity of young women to coronary disease.

Hypertension and coronary disease

Our series of 78 males and 49 females below the age of 55 years with myocardial infarction were reviewed for a history of hypertension. Thirty-three (67 per cent) of the 49 females and twenty-five (32 per cent) of the 78 males had a history of moderate to severe hypertension preceding the infarction. These results are in good agreement with the study of hypertension and coronary occlusion recently reported by Master (56). He found that 28 (70 per cent) of 40 women below the age of 55 with myocardial infarction had hypertension, and 26 per cent of the males with myocardial infarction before the age of 55 had a history of hypertension. According to Master, most of the previous studies relating to hypertension and coronary disease did not consider the steady rise in blood pressure of the normal population with age. Consequently many patients with myocardial infarction were classified as hypertensive although their blood pressures did not exceed the average pressure for the same sex and age group. In a previous study, Master and his associates (57) reported that 64 per cent of the males and 81 per cent of the females with myocardial infarction had a history of

TABLE 3

Normal Range of Blood Pressure and Lower Limits in Hypertension, as Newly Defined by Master

(Reproduced with permission from Master, A. M.: Hypertension and coronary occlusion, *Circulation* **8:** 170, 1953.)

Age (yrs.)	Normal Range (mm. Hg)		Hypertension Lower Limit		Age (yrs.)	Normal Range (mm. Hg)		Hypertension Lower Limit	
	Male	Female	Male	Female		Male	Female	Male	Female
	Systolic Blood Pressure					*Diastolic Blood Pressure*			
16	105–135	100–130	145	140	16	60–86	60–85	90	90
17	105–135	100–130	145	140	17	60–86	60–85	90	90
18	105–135	100–130	145	140	18	60–86	60–85	90	90
19	105–140	100–130	150	140	19	60–88	60–85	95	90
20–24	105–140	100–130	150	140	20–24	62–88	60–85	95	90
25–29	108–140	102–130	150	140	25–29	65–90	60–86	96	92
30–34	110–145	102–135	155	145	30–34	68–92	60–88	98	95
35–39	110–145	105–140	160	150	35–39	68–92	65–90	100	98
40–44	110–150	105–150	165	165	40–44	70–94	65–92	100	100
45–49	110–155	105–155	170	175	45–49	70–96	65–96	104	105
50–54	115–160	110–165	175	180	50–54	70–98	70–100	106	108
55–59	115–165	110–170	180	185	55–59	70–98	70–100	108	108
60–64	115–170	115–175	190	190	60–64	70–100	70–100	110	110

hypertension. However, they defined hypertension as any pressure exceeding 150 mm. Hg systolic or 96 mm. Hg diastolic. Under Master's new criteria of hypertension, based on an extensive study of the population, these values would be normal for some age groups (Table 3).

Hypertension appears to be an important factor in the development of coronary disease in the female. In both the female and the male the incidence of hypertension in the coronary group exceeds that in the normal population. This condition must certainly accelerate the atherosclerotic process even though it may not be the initiating factor (58).

Other diseases associated with coronary disease

Certain diseases are associated with a high incidence of atherosclerosis and coronary disease. In these conditions, the incidence in males and in females appears to be about equal. Two important examples are familial xanthomatosis (18) and diabetes mellitus (21), which are accompanied by high blood lipid levels for both sexes.

C. *Comment*

The findings of this report indicate that atherosclerosis resulting in coronary occlusion could be the end-product of several different processes. Theoretically, the role of all clinical factors related to the atherosclerotic process may be explained through 4 basic physiologic processes, which include time for development, the nature of the arterial wall, the level of serum lipids, and the level of

blood pressure. Many other authors have emphasized the importance of considering these basic elements in the study of atherosclerosis (3). These 4 factors appear to be additive to some degree, and the extent to which each contributes will determine the final degree of atherosclerosis. Equal amounts of atherosclerosis might develop from a slight abnormality in each factor or from a marked abnormality in one factor. For example, a pathologic change in the intima of an artery could cause deposition of lipids in the presence of a normal blood lipid concentration and normal blood pressure. Abnormally high levels of serum lipids could promote deposition of lipid even in normal arteries. Elevated blood pressure could increase filtration and deposition of lipids without other abnormalities. Moreover, the longer the arteries are acted upon by the atherosclerotic factors, the greater will be the amount of atherosclerosis developed.

The findings on the incidence of coronary disease according to age and sex may help to evaluate the importance of each of the 4 basic factors involved in atherogenesis. The increased incidence of coronary atherosclerosis with age may be partly explained by the time factor, but blood lipoprotein levels and blood pressure must also contribute, since they increase with age. The difference in the incidence of coronary atherogenesis between the male and the female may result either from a difference in the blood lipid levels or from a difference in the state of the coronary arteries. Several authors have suggested that estrogens may protect females from coronary atherosclerosis because of their effect on the level of blood lipoproteins or by a direct effect on the arterial wall. Dock (59) and Minkowski (60) have reported that at birth the intima of the coronary arteries is thicker in males than in females. This thicker intima might establish a background for the more rapid development of coronary atherosclerosis in the male, and lend support to the evidence for an arterial factor in the atherosclerotic process.

The studies on hypertension and myocardial infarction presented here further clarify the role of blood pressure as a factor in coronary atherosclerosis. The incidence of hypertension in males and in females with myocardial infarction exceeds that in the normal population. However, since more of the other factors leading to atherosclerosis at an early age exist in males, myocardial infarction without hypertension develops more often in men than in women.

In diseases such as diabetes mellitus and familial xanthomatosis all of the serum lipids are elevated to such levels that atherosclerosis usually develops at an early age regardless of the sex. Similarly, atherosclerosis may be induced experimentally in animals by feeding high cholesterol diets which cause extreme elevation of the serum lipid levels.

More extensive studies on the incidence of atherosclerotic coronary artery disease according to sex and age are needed. Such studies would undoubtedly lead to a clearer understanding of the relative importance of the various factors involved in the development of the disease.

III. HYPERTENSION AND HYPERTENSIVE CARDIAC DISEASE

The importance of hypertension as a clinical condition is well recognized. Along with arteriosclerotic cardiovascular disease, hypertension-induced diseases

TABLE 4

*Classification of Hypertension**

I. Pulmonary Hypertension
II. Systemic Hypertension
  A. Systolic Hypertension Only
    1. Thyrotoxicosis
    2. Anemia
    3. Heart block
    4. Arteriovenous fistula
    5. Psychogenic
    6. Atherosclerosis of the aorta
  B. Combined Systolic and Diastolic Hypertension
    1. Renal
      a. Pyelonephritis
      b. Glomerulonephritis
      c. Congenital lesions
      d. Obstructive lesions
    2. Endocrine
      a. Acromegaly
      b. Adrenocortical hyperfunction
      c. Pheochromocytoma
    3. Neurogenic
      a. Brain tumor (rapidly expanding)
      b. Cerebrovascular accidents
      c. "Diencephalic syndrome"
      d. Poliomyelitis
      e. Psychogenic
    4. Unknown etiology
      a. Essential hypertension
      b. Eclampsia
    5. Miscellaneous
      a. Coarctation of the aorta
      b. Increased intravascular volume

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constitute one of the greatest causes of death in the United States. Because of the chronic nature of most cases, the incidence of hypertension in the United States is much greater than indicated by the 320,000 deaths attributed to it yearly (61). The true incidence of hypertension is even more difficult to determine than that of coronary heart disease, for several reasons. A true sampling of the total population is hard to obtain. Blood pressure readings are often in error because they vary with the emotional state of the subject at the time of the reading, the hour of day, the opinion of the recorder regarding sounds, the nutritional state of the subject, and the physical state of the arteries. Definition of hypertension differs with almost every author. Because of the large variety of factors altering blood-pressure readings, and because definitions of hypertension vary, only broad generalities may be stated as to the incidence of hypertension among the population.

The causes of hypertension are protean (Table 4), and all of them cannot be discussed in a paper of this nature. By far the most common type of high blood pressure is essential hypertension, a condition of unknown etiology constituting 80–85 per cent of all hypertensive disorders (62). Many theories have been proposed to explain the mechanism of this disease (63–67), but the question of etiology is by no means settled. The chronically elevated blood pressure of essential hypertension has multiple deleterious effects, especially those involving damage to the heart, kidneys and brain (68, 69).

Although the damage produced by long-standing elevated blood pressure is recognized, the level of blood pressure which should be classified as hypertension is open to question. The definition of hypertension used is of utmost importance in the consideration of its incidence according to age and sex. The use of a rigid definition of the limits of normal blood pressure for all age groups and for both sexes has been questioned recently. Should a blood pressure of 150/90 mm. Hg be considered the upper limit of normal for females over 70 years of age, when 70 per cent of such women have blood pressures exceeding that value (70)? Should the same blood pressure limits be used for males and females in a certain age group, in view of the fact that the average readings for the two sexes differ considerably? An even more important consideration in defining hypertension is the question of what level of blood pressure will produce deleterious effects on the various organ systems if maintained for a considerable period of time. This question is of extreme importance in the prognosis and treatment of hypertension, but there is much disagreement regarding the answer.

The presently accepted blood pressure readings have become firmly established by the insurance companies (71). These values were derived from the early work of Bruton (72), Cook (73) and Janeway (74), and they have remained the standard limits to the present time. However, Bechgaard (69), Blood and Perera (75), Burgess (76), Alvarez (77), Diehl and Sutherland (78), and Master, Dublin and Marks (79) have demonstrated that patients who are classified as hypertensive may show no clinical symptoms for many years. These authors, therefore, have urged a reclassification of the limits of normal blood pressure. Master and associates (71, 79, 56) have offered new definitions of normal blood pressure and hypertension based on their study of 74,000 working men and women between the ages of 16 and 65 years. Table 3 shows the normal blood pressure and the lower limits in hypertension, as proposed by these authors. Hamilton and associates (80, 81), after another extensive survey of the population, have reached conclusions similar to those of Master regarding blood-pressure limits.

On the other hand, Robinson and Brucer (82), Perera (83), and others (84) have emphasized the importance of maintaining the previously set lower limits for hypertension, from a prognostic standpoint. This concept may be supported by a comparison of the hypertensive deaths in this country with those in Oriental countries (61). The upper limits of blood pressure in people of the Oriental countries seldom exceed 140/90 mm. Hg, and the number of deaths resulting from hypertensive cardiovascular disease is extremely low when compared with those in the United States.

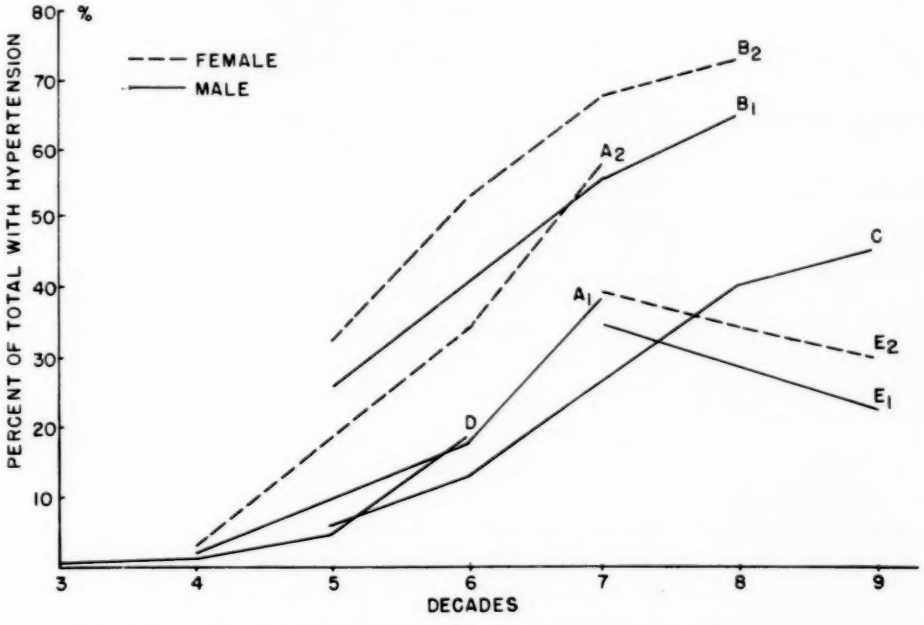

FIG. 5. Incidence of hypertension by age. (Reports of various authors.)

Author & Ref. No.	No. of Patients	Lower Limit of Hypertension (mg. Hg)	Sex
A_1 Life Extension Exam. (85)	6,975	150/100	M
A_2 Life Extension Exam. (85)	3,025	150/100	F
B_1 Master *et al.* (70)	14,849	150/90	M
B_2 Master *et al.* (70)	14,849	150/90	F
C Russek *et al.* (86)	5,331	150/95	M
D Levy *et al.* (87)	22,741	150/90	M
E_1 Monroe (88)	4,088	/90	M
E_2 Monroe (88)	3,913	/90	F

Figure 5 shows the incidence of hypertension in the later decades of life as reported by several authors. Other authors have reported incidences by age similar to those shown (80, 81, 89, 90). The results vary considerably depending upon the lower limits of hypertension used, the sex studied, and the group selected. These findings indicate that accurate incidences according to age-group have not been established. Studies by the Life Extension Examiners (85) and by Master and his associates (70) probably represent the most valid studies of the incidence of hypertension from the standpoint of an adequate population sampling. Essential hypertension appears to be rare in people below 40 years of age. According to Platt (91), severe hypertension below the age of 40 is usually secondary to another disease. However, Boynton and Todd (92) reported that 6–7 per cent of 43,800 males between the ages of 18 and 25 years had blood pressures exceeding 140/90 mm. Hg. According to Master's new definition of hypertension, the true incidence of hypertension would be much lower than those previously reported.

TABLE 5

Incidence of Hypertension in Males and in Females

Authors & Reference No.	Number of Cases	Per Cent Hypertension		Age Group	Lower Limit of Hypertension (mm. Hg)
		Male	Female		
Boynton & Todd (92).	75,218	7.3	1.4	18–25	140/
	75,218	6.1	2.5	18–25	/90
Alvarez (77).....	15,934	20.0	2.7	25	140/
Symonds (93).....	162,356	5.7	3.5	16	140/
Bowers (94).....	461	10.0	13.0	40–70	150/90
Master *et al.* (70).....	14,849	40.9	50.7	40–90	150/90
Gager (95).....	2,000	12.6	16.1	All ages	140/90
Wetherby (96).....	5,540	15.1	21.6	All ages	150/
Schwab & Schulze (11).....	10,188	3.4	10.6	All ages	150/95

Instead of the high incidences reported by Master *et al.* (Fig. 5) on the basis of the usual limits of hypertension, the incidences would be 3 per cent in the fourth decade, 6 per cent in the fifth decade and 10 per cent in the sixth decade on the basis of their new definitions. Although most reports indicate that the blood pressure increases with age, Monroe found a decrease in hypertension beyond the age of 70 (88). This study should not be overlooked because it includes a significantly larger number of people beyond 70 years of age than do most other studies.

Table 5 records the incidence of hypertension according to sex as reported by several authors. Figure 5 shows the incidence between the sexes in extensive studies of the later decades of life. Before 25 years of age the incidence in males exceeds that in females (77, 92, 93). However, after the age of 40 years, (according to most authors) the incidence in females exceeds that in males, though the increment is not large enough to suggest factors involved in the etiology.

Although the incidence of hypertension is greater in females, the sequelae affect males more commonly. The male is more likely to have the malignant form of hypertension (69, 97–99). This finding is surprising in view of the frequency of chronic pyelonephritis in most series and the general assumption that pyelonephritis is more common in females (100). However, most of the studies which indicate a greater likelihood for the development of malignant hypertension in the male were carried out on relatively small numbers of patients. White (18) states that clinically manifest hypertensive heart disease occurs about equally in both sexes. Blackford and Wilkinson (101) found that the mortality rate after ten years of hypertension was twice as high in men. This increased mortality in men may be intimately associated with the accelerating effect of hypertension on the atherosclerotic process, which is greater in the male. The fact that females have more hypertension than males should be considered when evaluating the findings that hypertension is associated with coronary artery disease more often in the female than in the male.

IV. OTHER CARDIOVASCULAR DISEASES

A. *Congenital heart disease*

The incidence of congenital defects of the heart and blood vessels is not high compared to that of the 2 major cardiovascular diseases, but the interest and challenge they pose is as great in many respects (102). With the recent advances in the field of cardiovascular surgery, and with our increasing knowledge of some of the underlying causes of congenital heart disease, there has been renewed interest in the incidence and diagnosis of these defects (18). Congenital anomalies may be inherited (103–105) or caused by a defect acquired during fetal life (106–108). The latter form is of special interest because the discovery of the causes of these acquired defects offers an opportunity to reduce the incidence of congenital cardiovascular disease.

An accurate estimate of the incidence of congenital cardiovascular disease among the general population is not available (109). Three general methods of determining the incidence of combined congenital heart disease have been employed, which include estimates of defects at birth (110), incidence in patients examined post mortem (103, 111, 112), and incidence derived from examination of school children. The examination of school children probably affords the most accurate statistics regarding congenital heart defects among the general population, but this does not necessarily represent the true incidence at birth (109). According to Packard and associates (113), the reported incidence of congenital heart disease in school children ranges from 0.07 per cent (114) to 0.60 per cent (115), but more likely is between 0.25 and 0.50 per cent (113, 116, 117). MacMahon, McKeown and Record (109) observed an incidence of 0.32 per cent in 194,418 births, which is in agreement with the results of studies on school children.

A review of 1028 cases of congenital heart disease was made for this paper. These cases were taken from a children's hospital, and the majority of the diagnoses were confirmed by autopsy, cardiac catheterization, or cardiac surgery. However, 202 cases were left unclassified because of incomplete diagnosis. Abbott (118) has published a well known study of 1000 cases of congenital heart disease. A comparison of the incidence and distribution of the various abnormalities between her 1000 cases and our 1028 cases is of interest. In Table 6 is a comparison of the incidence of congenital anomalies according to sex, for the 2 series. Although the number of cases in each category is not large, there is remarkable agreement between the 2 studies for the most part. Coarctation of the aorta, anomalies of the semilunar cusps, and transposition of the arterial trunks predominate in the male, and patent ductus arteriosus and atrial defects predominate in the female. Several authors have supported the trends appearing in these 2 series (109, 118, 119), but the findings should not be considered conclusive until larger series are studied.

Almost all authors agree that the total incidence of congenital cardiovascular anomalies is about equal for both sexes (18, 109, 111, 118–120). Of the 1028

TABLE 6

Incidence of Various Congenital Cardiovascular Anomalies According to Sex in 2 Series of Patients

Classification of Defect	Abbott's* Series			Present Series		
	Male	Female	Total	Male	Female	Total
Simple dextrocardia	10	6	16	15	7	22
Dextrocardia; situs inversus	3	4	7	0	3	3
Defects of intraauricular septum	32	39	41	14	22	36
Patent foramen ovale	15	24	39	5	9	14
Defects of intraventricular septum	29	29	58	100	81	181
Compete defect of cardiac septa	17	8	25	12	18	30
Persistent truncus arteriosus	11	7	18	12	7	19
Transposition of arterial trunks	42	18	60	42	24	66
Pulmonary atresia	17	10	27	14	17	31
Aortic stenosis and atresia	20	13	33	—	—	—
Eisenmenger complex	—	—	—	7	7	14
Anomalies of semilunar cusps	34	5	29	—	—	—
Triscuspid stenosis	1	2	3	11	21	32
Mitral stenosis	3	3	6	9	9	18
Patent ductus arteriosus	36	61	97	41	85	126
Coarctation of aorta:						
infantile type	4	2	6	26	12	38
adult type	53	15	68	9	4	13
Tetralogy of Fallot	—	—	—	59	56	115

* Reference 118.

patients in our series, 521 were males and 507 were females. This equal sex distribution for combined congenital heart defects supports the theory that neither sex has an inherently inferior cardiovascular system. However, the findings of Dock (59) and Minkowski (60)—that male infants have thicker coronary arteries than female infants—may partly explain the greater incidence of coronary artery disease in the male.

B. *Rheumatic heart disease*

Most cases of rheumatic heart disease begin between the ages of 4 and 15, with the height of onset between the seventh and eighth year (18, 121). The incidence depends upon the area of the country studied; it is about 1 to 2 per cent among school children in areas where rheumatic fever is prevalent (122–124). Development of the disease is rather rare after 20 years of age.

Both sexes are affected by rheumatic heart disease, but most authors agree that it develops more often in females than in males (121, 125). Ninety-one cases of rheumatic heart disease were reviewed for this paper. In accord with reports in the literature, 59 (65 per cent) of these patients were females, and 32 (35 per cent) were males. This is an interesting finding in view of the fact that the incidence of rheumatic fever is virtually identical for both sexes (126).

C. *Atrial fibrillation*

Atrial fibrillation is one of the most common and important of the disorders of cardiac rhythm. Common causes of the arrhythmia are rheumatic heart disease, hypertensive heart disease, thyrotoxic heart disease, and coronary artery disease (127).

For this report, 93 consecutive cases of atrial fibrillation were studied with respect to incidence by age and sex. Sixty-two (67 per cent) of the 93 patients were males and 31 (33 per cent) were females. The height of incidence was in the sixth decade for males, and in the seventh for females. Rheumatic heart disease, the chief known cause of atrial fibrillation, is more common in the female; thus the greater incidence of coronary disease in the male cannot account for the high ratio of males to females. White (18), who found a similar male-female ratio, suggested that greater strain in the male might explain this difference. However, more knowledge of the mechanisms producing atrial fibrillation is necessary before the 2:1 ratio can be explained.

V. SUMMARY

This paper has been concerned with those cardiovascular diseases which are most common, and those for which knowledge of the incidence by sex and age-group might add to a better understanding of the etiology. Many of the cardiovascular diseases not discussed here are secondary to other disorders, and their incidence depends upon that of the primary disease. For example, syphilitic heart disease is more common in the male because syphilis is more prevalent in men (128, 129), and the same relationship is true for several of the functional heart diseases resulting from coronary artery disease (18).

In this review of the incidence of cardiovascular diseases certain observations have been made which offer a better explanation for the causes of these disorders. The difference in incidence of coronary artery disease between the sexes suggests certain endocrine factors in the development of atherosclerosis. The role of serum lipoproteins in the atherosclerotic process is supported by the difference in the findings between males and females. The accelerating effect of hypertension on coronary atherogenesis is emphasized by the fact that coronary disease is rare in females less than 55 years of age without hypertension. Moreover, in conditions (*e.g.*, lack of ovarian function or diabetes mellitus) in which there are no sex differences with respect to endocrine factors and blood lipid levels, there are also no sex differences with respect to coronary atherosclerosis. A better understanding of the factors leading to atherosclerosis will facilitate the control of this disease.

A study of the incidence of essential hypertension contributes less to the understanding of its etiology than does a study of coronary disease. There is no marked difference in the incidence of essential hypertension between males and females. However, the rarity of the condition before 40 years of age and its rapid increase in the population after that age should be considered.

The difference in incidence of various congenital heart diseases between the

sexes is of interest, but the reasons are not understood. The sex ratio (equal) among patients with combined congenital heart defects suggests that neither sex has a circulatory system inferior to the other. The obvious difference between males and females with respect to coronary artery disease has led many to believe that the male possesses a weaker cardiovascular system than the female. The unexplained predominance of auricular fibrillation in the male might support such a concept, but the more common occurrence of rheumatic heart disease in the female would refute it. At present, there is no strong evidence to indicate any difference in the circulatory systems between the sexes, provided external factors are excluded. A continued search for the external factors which upset this balance will eventually lead to the cure or control of most cardiovascular diseases.

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ETIOLOGY OF SEVERE OBESITY: A STUDY OF FIVE CASES

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Obesity is a disease of unfortunate victims of either food addiction beyond body needs or disturbed metabolism favoring deposition of fat. It may be the sequela of illness, of a chance inherent gene, or of a myriad of stimuli that derange hypothalamic appetite control, metabolic pathways and enzymatic processes. It cannot be explained simply by a surplus of calories (1–3).

Over the years, stumbling blocks in controlling obesity (and the numerous commercial enterprises which feed upon it) have been many. These include: failure to uncover the missing links in an endocrine-metabolic pattern, associated with a lack of sensitive laboratory procedures; difficulty in handling associated socio-psychologic factors and their interpretation; lack of adequate controls; and complacency with known methods.

Treatment of obesity at present consists chiefly of a strict reduction in caloric intake, the use of drugs and other measures to curb appetite, thyroid therapy and other medication for which there is no clear indication, removal of water from the body, correction of socio-psychologic problems, group therapy, and the use of persuasion or motivation (4–5). The obese person often responds temporarily, only to return to the same sad state and to seek new panaceas. The recurrent cycles of weight loss and gain are perhaps analogous (2) to those in the hypothalamic obese animal (3) receiving a reducing diet: There seems to be a level beyond which weight loss leads only to renewed hyperphagia and the consequent recurrent gain in weight.

Substantial losses of weight in patients studied under constant regimens have been reported. How long these losses were maintained and whether medication or new dietary habits may have ultimately altered the metabolic picture or the appetite centers, is unknown at present. Short describes a woman who lost 259 pounds over a two-year period, at a rate of about ten pounds a month; her weight at the onset of treatment was 489 pounds (6). Short's regimen consisted of the usual unspectacular 600–1000 calorie diet, including 1 gram of protein per kilogram of body weight, small feedings between meals, dexedrine, diuretics —and the magic of teamwork. Recently Simeons (7) reported a form of treatment, open to debate or confirmation, consisting of daily injections of chorionic gonadotropin and a 500-calorie diet. In many patients this resulted in a loss of 1 to 2 pounds per day and an abatement of varying associated ills; there were no apparent harmful effects. For the most part, however, it appears that low-calorie diets do not curb the basic disease process in severe obesity and the imposed semistarvation may further damage the health of the patient.

The present report concerns 5 extremely fat women who were carefully studied

TABLE 1

TABLE 1

Pertinent Data on 5 Obese Women

Patient & Age	Family History	Weight Trends			Associated Conditions	Endocrine System				Cardiovasc. System	Central Nervous System	Hyperphagia—Diet
		Max. Wt.	Wt.	At Age (yrs.)		Gonad-Pituitary	Thyroid	Adrenal-Pituitary	Pancreas			
		(lbs.)										
M. G., 49	Father obese	403		8	"Typhoid fever"	Spontaneous abortion	Simple goiter No symptoms BMR + 4% Serum cholesterol, 287 mg./100 ml. PBI* normal	Slight facial hirsutism (postmenopausal) 17-KS** normal Sella turcica normal ←G.T.*** normal→	No glycosuria	L. Axis deviation; Blood pressure labile; max. 170/110	Hyperostosis frontalis; "nervous"	Large quantities food
				11–12								
				16	Goiter; "miscarriage"							
			149	18								
			190	18½	Inflammation rt. hip; (bed one month)							
				21	"Mumps"							
			300	28	Pyelonephritis							
				38	Pelvic inflamm. disease Menorrhagia; surgery							
			463	48	Surgical menopause							
			335½	49	(diet)							
B.C., 29	Mother obese	419		Stout as child		Pregnancies Gonadotropin excretion values unreliable Libido "normal"	No symptoms BMR +35.6% Ser. chol. 282 mg./100 ml. PBI normal I^{131} uptake (thyroidal) normal	Cushing-syndrome-like appearance 17-KS normal Sella normal ←G.T. normal→ Grossly, no tumor	No glycosuria	B.P. 130/80–160/110	"Family problems"	Copious intakes; starches, fats
			190	18								
			210	21	From catamenia							
			295	24	1st pregnancy							
				25	"Miscarriage"							
			397	27	3rd pregnancy							
			397	29								
J. H., 24	Mother obese	364		3	Malaria	Gonadotropin excretion normal	No symptoms BMR + 5% Ser. chol. 228 mg./100 ml. PBI normal I^{131} uptake normal	17-KS, 23.5 mg./24 hrs. Sella normal ←G.T. normal→	No glycosuria	B.P. 100/60–185/135	Encephalitis, recurrent; nervousness	Increased appetite; increased intake
				7	Severe tonsillitis							
				Gain of 25 lbs in 1 mo.	tonsillectomy; complications. Bed rest							
					Encephalitis							
				Continued gains	Encephalitis; recurrences over 10 yrs.							
M. L., 45	Mother obese diabetic; Father obese	274½	80–90	From 1 on	Severe eczema; drugs	Hypomenorrhea Gonadotropin excretion normal	No symptoms BMR −4% Ser. chol. 412 mg./100 ml. PBI normal I^{131} uptake normal	17-KS normal Sella normal ←G.T. normal→	No glycosuria	B.P. 140/90	Nervousness	Copious intake; preference for sweets
				10								
				10–11	Catamenia							
			180	by 17								
			Gain of 100 lbs.	35	Immobilization 25 mo., for fractures; hypomenorrhea							
			250	40								
I.P., 32	—	340	Sudden onset		Menorrhagia; pelvic inflamm. disease	Pregnancies "Benign uterine hyperplasia" Gonadotropin excretion normal	No symptoms BMR + 18.5% Ser. chol. 287 mg./100 ml.	17-KS normal Sella normal ←G.T. normal→	No glycosuria	B.P. 190/110–200/120;	No manifestations	"No appetite"
			326	30								

* PBI = serum protein-bound iodine level. ** 17-KS = 17-ketosteroids (urinary). *** G.T. = Glucose tolerance.

in our clinic, particularly for possible clues as to the development of the obesity (Tables 1, 2 and 3).

CASE HISTORIES

Case 1

M. G., a 49-year-old woman, weighed 403 pounds on her first visit to the clinic. She admitted freely to a hearty appetite and to nervousness. She could recall no member of her family with obesity, other than her father.

She became "sluggish" after episodes of "typhoid" fever at ages 8 and 11–12 years. Overweight was first apparent at 16 years. A simple goiter was noted at this time; also a "miscarriage" occurred following out-of-wedlock pregnancy. By the age of 18, she weighed 149 pounds. Her weight continued to rise during periods of illness; these were mostly of an infectious nature, and at times required extended periods of bed rest (Table 1). By age 38, following hysterectomy and bilateral ovariectomy for menorrhagia, her weight had risen to 300 pounds.

This patient suffered from mental "depression," which was at least in part related to her husband's death from leukemia. She was referred to the neuropsychiatry service for help with this problem. X-ray examination of the skull revealed nothing abnormal except for hyperostosis frontalis.

The possible elements involved in the development of obesity in this patient include:

1. Constitutional factor (obese father).
2. Habitual overeating.
3. Prolonged bed rest.

TABLE 2

Summary of Findings

Patient & Age	Known Obesity in Family	Type of Onset of Obesity	Maximum Weight (lbs.)	Overeating	Nervousness	Events Coinciding with Gains in Weight	Remarks
M. G.,49	Father	Gradual	403	Yes	Yes	Miscarriage; simple goiter; severe infections; menorrhagia; surgical menopause	Hyperostosis frontalis; minimal facial hirsutism
B. C., 29	Mother	Gradual	419	Yes	Yes	Catamenia; pregnancies; amenorrhea	Proteinuria; adenoma right lung
M. L., 45	Mother, Father	Gradual	274½	Yes	Yes	Catamenia; immobilization; hypomenorrhea	Chronic, severe eczema; prolonged medication; mother diabetic
J. H., 24	Mother	Gradual	364	Yes	Yes	Severe infectious disease; central nervous system involvement	Encephalitis
I. P., 32	None	Sudden	340	No	No	Menorrhagia	Hypertension

TABLE 3
Blood Values

Patients	Dates	Hemoglobin (Gm./100 ml.)	Hematocrit (%)	Other Values
M. G.	Jan. 12, 1953	15.4 (98%)	44	WBC 7,900
B. C.	Mar. 4, 1952	19.2 (123%)	56	RBC 5,980,000 MCV 93 MCH 32 MCHC 34 WBC 9,800
	Aug. 6, 1952	16.5 (106%)	52	WBC 9,300
	May 8, 1953	—	52	
M. L.	Aug. 24, 1954	15.0 (96%)	—	PCV 46 WBC 10,000
J. H.	Aug. 10, 1954	15.2 (98%)	—	PCV 47 WBC 14,200
I. P.	July 23, 1951	13.6 (87%)	—	
	Nov. 13, 1952	12.7 (81%)	—	
	Sept. 29, 1954	12.4 (79%)	—	
	Oct. 6, 1955	13.3 (85%)	—	WBC 7,900 PCV 41

4. Infections and other traumata.
5. Endocrine factor.
6. Hypothalamic factor

M. G. was one of 3 patients who reduced her weight consistently while at this clinic. She lost 67½ pounds in one year while receiving an 800-calorie diet and amphetamine.

Case 2

B. C. was 29 years old and weighed 397 pounds. Her "buffalo" appearance, plethoric facies, mild facial hirsutism, purple striae, and edema of the lower extremities clinically suggested Cushing's syndrome, but this was not confirmed. Her blood pressure was only moderately elevated on a few occasions.

As in the case of M. G., 1 member of her family, her mother, had been obese. Both of B. C.'s children were normal in weight and appearance; unlike their mother, they were mentally alert.

B. C. was "stout" as a child, always a copious eater, with a definite preference for fats and carbohydrates. Following the onset of catamenia, her weight rose and by age 18 she weighed 190 pounds. With pregnancies (2 normal and 1 terminating in spontaneous abortion) her weight increased nearly "100 pounds" on each occasion. Six months after her last pregnancy, amenorrhea developed.

Other than the relationship to pregnancies and amenorrhea, there was no clear-cut evidence of endocrine involvement in association with the obesity (Table 1). The urinary gonadotropin titer was difficult to interpret because of marked proteinuria, the cause of which was not ascertained. The level of blood protein was normal; an intravenous pyelogram was "probably" normal; and the results of a Bence Jones protein test were negative. The

Addis urinary cell count and the results of routine urine examinations suggested latent glomerulonephritis, but this was not substantiated later by the coroner's findings.

Possible causes of the obesity in this case include:

1. Constitutional factor (obese mother).
2. Hyperphagia plus nature of diet.
3. Inactivity.
4. Hypothalamic factor.
5. Endocrine factor.

B. C. was the only one of the 5 patients studied in whom the blood count, hematocrit (Table 1), and symptoms were consistent with the inaccurately named "Pickwickian syndrome" (8, 9).

She died suddenly from gastric hemorrhage of undetermined origin at 29 years of age. Grossly, the endocrine glands showed no abnormalities. However, with the exception of the ovaries, neither the endocrine glands nor the hypothalamus were studied microscopically. The secondary amenorrhea and the proteinuria were not explained by the postmortem findings.

Case 3

M. L., a 45-year-old woman, weighed at the maximum, 274½ pounds. She admitted being a hearty eater, particularly when "upset," with a preference for sweets. Her mother was an obese diabetic, her father was "moderately" obese, and 1 of the other 4 siblings was "slightly" obese. The body build of her grandparents was not known.

Especially noteworthy in the patient's history was chronic eczema with lichenification from the chest upward. This disease had its onset at 1 year of age and had been treated with a number of drugs. Obesity developed when she was about 11 years old and coincided approximately with the onset of catamenia. A weight of 180 pounds at 17 years of age was attributed by the patient to large doses of yeast tablets administered for the eczema. Another substantial gain in weight, about 100 pounds, occurred at 35 years of age, when fractures of the tibia and ankle necessitated immobilization for a total period of twenty-five months. Menses were regular and flow moderate until about the time of this last major weight gain, when hypomenorrhea developed.

The serum cholesterol level was markedly elevated. However, the patient showed no clear-cut evidence of thyroid disease (Table 1). She had received thyroid medication for a period of two years but had discontinued it one year prior to her care at this clinic. With this therapy, plus dietary restrictions and appetite depressants, she had lost 40 pounds. However, the 40 pounds were rapidly regained following an emotional "upset" and hyperphagia.

The possible causes of obesity in this case include:

1. Constitutional factor (obese diabetic mother, obese father).
2. Hyperphagia and habit.
3. Psychosomatic factor.
4. Endocrine factor.
5. Chemical factor.

Case 4

J. H. was an unmarried 24-year-old woman. On her first clinic visit she weighed 364 pounds, but lost 46 pounds consistently with therapy over four and a half months. Her blood pressure tended to be labile, ranging from 100/60 to 180/135 mm. Hg. Headaches and blood pressure appeared to decline with substantial weight loss.

Obesity had been known in her maternal grandfather's family. Her father was not obese; her mother became markedly obese following an artificial menopause at twenty-eight years of age.

The patient's obesity, associated with hyperphagia, first rapidly developed following

surgical removal of markedly hypertrophic and chronically infected tonsils at the age of 7 or 8 years. She gained 25 pounds during one month's hospitalization for postoperative complications. From then on, her weight rose steadily in association with frequently recurring episodes of high fever and unconsciousness, which lasted from fourteen to eighteen days at a time. These attacks, apparently due to an encephalitis, decreased in number and duration after a period of several years.

J. H. is the only one of the 5 patients studied who showed no apparent weight gain in association with gonadal changes. Pregnancy had occurred out of wedlock at 16 years of age and had terminated with a stillbirth.

A skull roentgenogram showed a normal sella turcica; there was a small 4-mm. area of calcification, presumably on the falx cerebri; the pineal gland was slightly calcified, but within normal limits in size. An electroencephalogram was "normal with more than usual fast activity."

Possible causes for the obesity of this patient include:

1. Constitutional factor (mother obese following surgical menopause, maternal grandmother's family obese).
2. Serious infectious disease.
3. Surgery, with postoperative complications.
4. Prolonged bed rest.
5. Central nervous system involvement (encephalitis).
6. Resultant hyperphagia.

Case 5

I. P., markedly obese, weighed 340 pounds at 32 years of age. Her case differed from the others in these respects:

1. Sudden onset of obesity at age 30.
2. Lack of known constitutional factor.
3. Lack of appetite and no increase in her food intake (according to her repeated assertions).
4. Persistent hypertension.

As in 3 of the other cases, a menstrual abnormality was noted in association with the gain in weight. Over a three-year period she had had recurrent menorrhagia on the basis of benign uterine hyperplasia. Earlier she had had 2 successful pregnancies.

In this case the only known factors possibly involved in the sudden onset of the obesity were endocrine (gonado-hypophyseal).

DISCUSSION

In these 5 patients with severe obesity, the following factors may have been either causative or associated with the disease process:

Factors	No. of Patients (out of 5)
1. Constitutional	4
2. Overeating	4
3. Diencephalo-hypothalamic	
a. Organic	1 or 2
b. Functional	4
4. Endocrine	
a. Gonado-pituitary	4
b. Other	?
5. Trauma (infection, surgery, drugs)	3
6. Inactivity	at least 3

In 4 of the 5 cases, at least 1 parent was known to be obese also—whether from habit, heredity, or other causes. Only 1 parent was in addition, diabetic. That heredity may play a role in obesity has been amply demonstrated by animal studies (3, 10–12), as well as by human statistics relating to twins and families (13–14). Obesity in the yellow strain of mice was first noted by Danforth in 1927; it is carried by a dominant gene (10). In 1950 Ingalls, Dickie and Snell discovered the hereditary obese hyperglycemic syndrome, due to a recessive trait in mice (11). In mice, the primary morphologic abnormality appears to be in the pancreas (3, 12, 15). Mayer and his associates observed a similar hereditary syndrome in Shetland shepherd dogs (3).

Four of the 5 patients studied were admittedly copious eaters, either because of hyperphagia or habit; at least 2 showed a preference for either starchy, sweet or fatty foods. Evidence of the importance of food intake, in quantity at least, in contributing to overweight and obesity is provided by the results of many balance studies and the classic work of Newburgh on caloric intake and output (16). Studies on hypothalamic-induced obesity show that obesity may be due either to hyperphagia (17–19) or to interference with the satiety mechanism (20) —linked respectively with each of 2 centers of appetite control, a feeding and a satiety center (21). Concomitant changes in fat metabolism may occur (22). There is a difference of opinion as to whether the mechanism of hyperphagia is humoral, nervous or gastric in origin. A new concept, much debated, of gluco-receptors in the hypothalamus which respond to the amount of glucose available has been proposed, based on at least circumstantial evidence (3, 21, 23). Other physico-chemical inter-reactions may ultimately prove to be the mechanism involved. Habit patterns may play a role, quite apart from hyperphagia, and merit investigation.

The metabolic setting may determine whether a person will or will not become obese as a result of hyperphagia and increased food intake, and is therefore of great importance in the development of this disease. This is evident from a consideration of hyperthyroidism (2). It is also conceivable that certain types of diets may eventually lead to obesity through induced metabolic changes; for example, by increased demands on the insulin requirement, with an effect equivalent to that of partial pancreatectomy (24). It is becoming more evident that, contrary to widely held tenets, the degree of physical activity bears a close relationship to weight gain and weight loss (3, 17, 25–26).

Four of the 5 patients in our study were under some emotional distress or suffering from nervousness. One of the patients had had episodes of encephalitis. That the central nervous system may be involved in the development of obesity is indicated by the results of experimental hypothalamic lesions and of hypothalamic stimulation (17–19), and by reports of obesity following prefrontal lobotomy (3, 27). The sudden onset of obesity subsequent to severe psychologic trauma (28) and brain injury (29) has also been noted. Lesions in the hypothalamus as a result of leukemic infiltration were found in a 5-year-old patient in whom hyperphagia and obesity suddenly developed during the course of lymphatic leukemia (30).

There are sporadic reports in the literature of severe obesity resulting from encephalitis (31–32), as suggested also by a case in our study. The mechanism is presumably diencephalo-hypothalamic. Likewise, the diencephalo-hypothalamus had been implicated as the source of obesity following pregnancy, in women bebetween the second and fourth decades (33). There are some reports indicating that the obesity associated with hyperostosis frontalis (34) may be due also to hypothalamic (35) if not endocrine (36) involvement, but this has long been disputed.

In 2 of our patients (M.G. and J.H.) development of obesity seemed to be correlated with the occurrence of infectious diseases, including encephalitis. The sudden appearance of obesity following infectious disease has been reported from time to time in the literature. The infections include pulmonary tuberculosis (37), tuberculous meningitis (38), mumps meningitis (39), scarlet fever (40), erysipelas meningitis (41), syphilis (42), and typhus fever (43). It is apparent that the central nervous system was involved in several of these reported cases. An increased demand on the pancreas has also been suggested as a possible cause for the obesity observed following certain infections and other stress conditions (44).

In our series there was no evidence of pancreatic disease except for a history of diabetes mellitus in 1 family. Involvement of the pancreas in obesity has been demonstrated in obese hyperglycemic mice (3, 12, 15, 45). Changes noted in the pancreas appear to be consistent with other findings which indicate excessive secretion of a hyperglycemic factor ("anti-insulin" hormone) as well as an increased secretion of insulin (15). Studies (a) on the role of insulin in fat synthesis (46–48), (b) on the obesity produced experimentally by prolonged use of protamine zinc insulin (49–50), and (c) on the frequent association of diabetes mellitus and obesity (51) also suggest the importance of an intact functioning pancreas in maintaining normal weight.

Abnormalities of other endocrine glands may also facilitate the development of obesity. When thyroid function is reduced in animals, either by thyroidectomy or by administration of propylthiouracil, forced feeding more readily results in obesity (52). Yet, the clinically obese, according to laboratory data (53–54), show no more evidence of thyroid disease than the non-obese. It would seem that the thyroid enters the picture merely as pacemaker; if habit dominates and does not permit adaptation to a changing rate of thyroid activity, then obesity may result. There was no clear-cut evidence of thyroid disease in any of the 5 women in our study. One patient (M.L.) had received thyroid medication but discontinued it one year prior to admission to the Clinic. Her serum cholesterol level (Table 1) was abnormally high, but other thyroid tests as well as her clinical status did not establish a diagnosis of hypothyroidism.

The appearance of 1 patient (B.C.) suggested Cushing's syndrome, but this diagnosis was not confirmed. The obesity in Cushing's syndrome and that resulting from prolonged use of corticotropin or cortisone (44) is well known. Contrariwise, obesity has been observed in surviving unmedicated adrenalectomized animals (55). Abnormalities in 17-ketosteroid excretion have been reported in

certain forms of juvenile adiposity (56–58), and an apparent hyperadrenocorticism in women with increased 17-hydroxycorticoid excretion has been attributed primarily to an enlarged steroid pool (59).

Evidence of direct pituitary involvement in obesity is suggested by the finding of a fat-mobilizing substance, "adipokinin," in an oxycel-purified corticotropin preparation (60). Hypofunction of the female pituitary has been suggested as a hereditary factor in the sterile-obese syndrome of the mouse (61).

Some correlation was noted between the development of obesity and gonadohypophyseal or primary gonadal changes in 4 of the 5 cases presented in this paper. Weight gains were associated with the onset of catamenia in 2, with pregnancies in 2, and with menstrual abnormalities (amenorrhea, hypomenorrhea or hypermenorrhea) in 4. Obesity in association with menstrual abnormalities (33, 62) and pregnancy (33) has been described in the literature. It has been found most frequently in conjunction with secondary amenorrhea, which, in turn, often improves along with loss of weight (62).

In the case history of 1 patient (M.L.), the question of prolonged drug administration in relation to obesity is briefly presented. Certain toxic substances in sufficient amounts may produce obesity, possibly through their effects on the hypothalamus or on systems directly involved in fat metabolism. Gold thioglucose will produce obesity in mice (63). This effect is apparently due to extensive hypothalamic injury involving the ventromedial nuclei (64). Other substances reported to produce obesity include arsenic, given in subtoxic doses (65), and conteban, administered to tuberculous patients (66). In patients with severe infectious disease such as tuberculosis or syphilis, it may be difficult to ascertain the significant trigger mechanisms leading to obesity—the infection *per se*, the therapeutic agent, the central nervous system involvement, the prolonged bed rest or the altered feeding patterns. The factor of immobilization should not be forgotten. However, it seems that unless the metabolic picture or habit pattern be changed permanently during periods of illness, there is a return to normal physiologic balance once the factors of bed rest and the processes requiring such rest are eliminated.

It cannot be too strongly stressed that careful autopsy studies, particularly with regard to the endocrine glands and the hypothalamus, may be of utmost value in understanding the development of severe obesity.

SUMMARY

Etiologic factors in the development of obesity are varied. Best established are those of relative caloric intake and energy expenditure. With respect to caloric intake at least, the central nervous system is involved, either because of organic disease and trauma or because of a "functional" state, as in habit patterns and neuroses. In addition, complex and varied metabolic factors may be involved, primarily or secondarily. Any or all of these mechanisms, hypothalamic or metabolic, may be triggered or altered by heredity, by toxic agents, by stress, by pregnancy, or by specific pathologic conditions such as infectious or invasive disease. The endocrine glands (hypophysis, thyroid, adrenals, gonads and pancreas) have been shown to be involved in certain forms of obesity.

A study of 5 extremely obese women was undertaken in relation to the various operative factors in this disease. It is hoped that the findings will stimulate other clinical and experimental investigations, revealing in time all the factors in the disease process.

In 4 of the 5 cases, at least 1 other member of the family was known to be obese, whether by heredity, habit or coincidence. Four of the 5 patients noted excessive "appetite"; only these 4 complained of nervousness or a nervous disorder. One of the 4 had suffered from central nervous system disease, in the form of encephalitis. In another patient, sudden precipitous weight gains paralleled attacks of severe infectious disease. In the latter 2 instances and in a third case, prolonged bed rest may have been either a causative or a contributing factor to the increase in weight.

In 4 of the 5 women, gains in weight paralleled physiologic (catamenia, pregnancy, menopause) or pathologic gonadal changes.

One of the 5 patients differed from the others in these respects: sudden onset of obesity, advanced hypertension, asserted absence of hyperphagia or overeating and of mental distress, and the absence of known obesity in her family.

The importance of including microscopic examination of the endocrine glands and of the hypothalamus in autopsy studies of the obese, is stressed.

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GERIATRIC SOCIAL WORK*

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Social work, as well as other professions, has always been concerned to some degree with the aged, but in the last decade the unprecedented increase in the number of the middle-aged and aged population has perforce focused the attention of our civilization on their needs and problems. It may be well to take a bird's eye view of the field, with emphasis on case work.

Social work is only one of the professions which, like theology, law or medicine, helps people in trouble on a case-by-case basis. Social casework has been defined in many ways, ranging from the highly technical to the popular lay definition. The essence of all definitions is that social casework is the process of helping a person who is in trouble stemming from his own inner conflicts and deficiencies or from a wide variety of environmental difficulties. The variety of human troubles has engendered the development of different foci of emphasis in the basic art of casework.

Thus we have practicing social workers in the fields of generic casework—medical, psychiatric, group, vocational, rehabilitation, community organization and research. They work in a variety of settings in many different capacities in either governmental or voluntary social agencies. In the governmental field they are employed in social welfare and in public health departments, schools and universities, housing projects, hospitals, correctional and protective agencies and institutions, and in recreational programs.

In the voluntary field, social workers are employed in family and child welfare agencies, counselling and guidance clinics, private hospitals, community centers, camps, institutions for children and for aged, and religious agencies and unions. The most recent development is the free-lance private practitioner. In many of these settings, there has been increasing concern with older persons and a growing body of specific knowledge about them as related to each of the settings. This body of knowledge could be all defined under the one heading of geriatric social work.

GERIATRIC SOCIAL WORK IN A HOME FOR THE AGED

I shall confine myself to my area of practice—generic social case work in an indisputably geriatric field, namely, a Home and Infirmary for the Aged. The Rosa Coplon Home and Infirmary, in line with the most recent trends, serves persons of relatively advanced age in the domiciliary wing and the chronically ill in the hospital wing. The former are aged people who, because of social factors or

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personality difficulties or both, need a degree of protection and control not possible in ordinary family life. The chronically ill are those who no longer qualify for treatment in general hospitals, but who are still in need of long-term nursing care which they cannot receive in their own homes or in the homes of their children. Often such patients are admitted directly from the hospital. They may be non-psychotic, mentally deteriorated patients, who are ambulant. They may be suffering from paraplegia, Parkinsonism, blindness, terminal carcinoma, or any combination of the degenerative chronic diseases.

What kind of worker is best suited for such a Home? The ideal would be one who has had experience in generic, medical and psychiatric disciplines and in group work. A knowledge of, and personal identification with the special cultural and religious background of the residents is most helpful. Such a paragon is not easy to come by, so often a Home has to accept one of less comprehensive attainment. Whatever her training and experience, she must be mature enough to have resolved her own negative attitudes regarding aging and death. She must have understanding, and acceptance of the motivations and emotional needs of old people specifically. She should realize that personality difficulties such as quarrelling, complaining, withdrawing or assaulting are defensive maneuvers on the part of the resident in his attempt at adaptation to an ever-changing internal and external scene.

It has been said that psychologically we are afraid of only one disease, that is, the dissolution of the ego. Not that residents in a Home for Aged are necessarily articulate in their fears of death. On the contrary, except for morbid curiosity at the immediate time of death of a fellow resident, they ignore the phenomenon; they seldom mention those who have gone from their midst. The social worker must understand that this fear of death, this shrinking, can only be met by a compensating expansion of the ego derived from new interests and activities. She must have a belief that aged people can live in the present, and that when everyday life is made more fascinating for them, the less inclination there will be to turn to the past and to dread the future. She should remember that the aged who are living in institutions constitute a very small percentage of the older persons in the comm unity, and that most old people outside of Homes lead relatively normal, full l'ves. It should be her goal to help create in the Home the possibility for a full life for each resident, to the full measure of his potential.

Let us consider the place and the function of the social service department and the worker in a Home for Aged. This depends upon the size of the agency, the administrative pattern, and the degree to which the Board, the administrator and the staff understand and accept social work. Indeed, in some instances, the Board and the co-workers demand the most skillful and thoughtful application of case work. This is especially true when social service is first introduced into a Home. There is no clear, defined area of responsibility. The worker must feel her way into her role on an experimental basis. Often she must tactfully demonstrate to the administrator, staff and residents how to use case-work services constructively. As in most sectarian Homes, she works in cooperation with a lay committee. Together they develop general policy and practices in the Home.

Whatever the set-up, the department of social service in a sense is the core of the Home. The social worker receives the requests for admission. After admission, the staff members look to the social worker for help in coping with the problems which individual residents present. The residents look to her for understanding and warm acceptance. Often they consider her as a special pleader.

Processing of admissions

One of the chief functions of the social worker in a Home for Aged is the processing of applications for admission. In general, there are 2 kinds of applications: 1) those made by the applicant himself, by his children or by interested persons, for admission to the well-residents group; and 2) those for admission to the Infirmary (by far the larger group), usually made by relatives, physicians, interested persons, or other agencies.

In the first group our consideration is whether the request is one that comes on the initiative of the applicant himself or whether it is the plan of his relatives. Even if the applicant comes in person, in 99 per cent of cases he comes reluctantly with fear in his heart—fear of the unknown and the untried—and with preconceptions of a Home as the last stopping place before death. The reasons given usually are that the applicant is no longer able, or thinks he is no longer able, to care for himself in his current accommodations. He (or she) is living alone and finds it most difficult to manage the daily routines of living, or else is living with relatives who find that this sort of plan is no longer bearable, either for him or for his children or for both.

Rarely now is the chief motive one of economic need. With social security benefits and with more flexible old-age assistance programs, almost every old person in the community can meet his basic needs of food, shelter and clothing, at least on a minimum basis. Medical care is available in the community for those who are still able to go to clinics or to private physicians. As more and more community services become available for the aged living in their own homes, fewer persons need to come into the Home. The current trend is to help oldsters live in the community as long as possible rather than in institutions.

If possible, the worker must get to the basic reasons which impelled the person to take this step, which for almost everyone is one of ambivalence and trauma. It may become apparent to the applicant or his relatives that the Home is not the best answer to the problems which face them, as they are not really ready for the separation. However, they may be in need of continued counselling with respect to their personal relationships or with respect to other concrete services such as financial, medical or recreational resources within the community. Then the case worker informs the applicant of those resources and, if desired, helps the client avail himself of them.

The exploratory process goes on at different paces with different individuals. If the old person, the family and the case worker are convinced that admission may be the best solution, the application is accepted for further study. During the interviews it is necessary to explore the physical, mental, emotional, social and economic status of the applicant so that the worker may present her findings

to the medical staff and to the social service committee if need be, for final decision regarding eligibility. During this process, the applicant is helped to articulate and face the fears and conflicts involved in separation from the known, and to take the first step in meeting the unknown which has so many unillumined hazards for him. The intake process is designed to be a foretaste of what it means to live in an institutional setting, perhaps sharing a room and certainly sharing various facilities with other residents. If the applicant is a woman and a housewife, it means ceasing to be boss in her own home and in her own kitchen and to eat food that is prepared without special consultation of her likes and dislikes.

The worker points out the reality situation in an institution, which is so different from living in a normal family relationship or living alone. Often the applicant's real feelings about his request and the prognosis for his adjustment are revealed in his responses. It may be that the client who most needs the Home has the most conflicts and fears about admission. If he is mentally competent, the worker must be able to sense his need for independence. Short of neglect and deprivation, she must respect such a client's hesitation and unwillingness to be admitted.

Sometimes even after it becomes clear to the applicant that he has better physical accommodations with his children than he can expect in a Home, his need to preserve his autonomy and self-assertion makes him choose admission. The case worker, recognizing the client's motivation, may recommend admission, although she realizes it may be for a short duration. This she does for the therapeutic effect that such a placement may have on both the client and his children. Such a case was that of Mr. B.:

Over a period of two years Mr. B. made periodic applications to the Home. It was evident to the worker, although he did not say so, that he usually came after a violent quarrel at home. He gave various reasons for his request, but never the real one. Once, it was because he was lonely and he had no one of his age to talk to. Another time, he said his daughter refused to cook the food that he likes, the son-in-law was not respectful, and the grandchildren disregarded him. Of the quarrels immediately preceding his visits there was never a word. His brother-in-law, who was a resident in the Home, stated that he was much more satisfied than when he lived with his daughter and son-in-law. The worker tried several times to involve the daughter and some of the other children in an application process without any success. Their father had a good home and it was he who was unreasonable and cantankerous. They felt they had stood it so long that they had no intention now of participating in any application for a Home; they would not be so disgraced. Another factor in their unwillingness was that their father was a man of considerable means and they naturally were interested in conserving them.

Finally, Mr. B came in a few months ago to demand his admission. He declared that he was unhappy in his daughter's home, he was of a sound mind, financially independent, did not have to consult his children, and he wanted to enter the Home. All he said was true, and as the children still would not come for consultation, he was admitted—much to the consternation of his family. Mr. B. expressed himself as delighted with the Home. At the time of his entry, the daughter with whom he had resided wailed and wept and tried to assuage her guilt by requesting special considerations for things which she imagined that he needed. The other children and grandchildren visited him constantly. After a month, in which Mr. B. confided to the worker he had seen more of his children and his grandchildren than in the previous five years, he allowed himself to be persuaded to return to his daugh-

ter's home, but not before she had promised to cater to his every wish and the son-in-law had made due apology. On leaving, surrounded by his family, he loudly assured the worker that the Home was wonderful, and that he was making a sizable donation; he was leaving only to please his daughter and if he didn't like the way he was being treated, he would return; she had better please him "or else." In this manner Mr. B. had asserted himself and had regained his lost ascendancy over his family. The prognosis for his remaining with his children is anybody's guess. The worker is keeping her fingers crossed.

However, more and more requests for admission to the Infirmary of the Home are made, not by the prospective residents but by their relatives or physicians. For instance, during the year of 1957 there were twice as many admissions for the Infirmary as for the domiciliary wing. More often than not, the prospective resident is incapable of making decisions. He is mentally or physically incompetent, or both, and is in need of protective custodial and nursing care. Necessarily, the basic principle regarding client autonomy must be waived in such instances. The relative becomes the real client.

More often than not the patient's cultural and religious tradition has so permeated his being that for many adult children the necessity of placing a parent in a Home creates a serious situation. The conflict over the breach of the fifth commandment of the Decalog is nigh insoluble without help. The adult child may not be sufficiently matured emotionally to free himself from his parent's domination, yet some action must be taken. The social worker tries to help in the maturing process. The following is a case in point:

Mrs. F. telephoned asking for an appointment. The worker could sense that she was suffering from great emotional stress. She preferred not to give any information over the telephone, saying that this was a very confidential matter and that she would like to talk to the worker as soon as possible. An appointment was given for the next day. However, Mrs. F. came very late. She opened the interview by saying that she was not intending to place her mother in the Home. On the way over she had wondered why she was coming and what she would tell the worker. She has been upset about her mother for a long time and had suffered great anguish. When a crisis arose, she often determined that she would follow her physician's advice to place her mother in a Home, but when it came time to ask for this placement she could not bring herself to do it. Her head told her it was wrong to continue keeping her mother in their own home, but her heart refused to sanction the separation.

Her mother (Mrs. O.) has been a problem to this only child (Mrs. F.) for as long as she could remember. Her parents' marriage was an unhappy one. Her father died young and the mother, who was a demanding, autocratic, immature, self-centered person, sought all her satisfaction through dominating the daughter's life. Until the daughter was able to earn a living, they had been supported by relief agencies. The only independent action the daughter ever took was her firm stand that she would be married, in spite of her mother's objections. After marriage, the mother (Mrs. O.) continued to live with the daughter and her husband and ruled the household. She resented the 4 children who were born to the family, and her resentment became greater with each. She no longer could maintain the primacy of interest, she no longer could claim her daughter's full attention. She interfered with the parents' discipline, she quarrelled with the children as if she were one of them. Within the preceding three years, since the birth of the youngest child, Mrs. O's judgment had become progressively worse, she was more nervous, more irritable, more self-centered and disruptive to the family life than ever before.

Physically, too, it was impossible to continue in the present set-up. For instance, the youngest child never could sleep a night through, because her room adjoined the grand-

mother's. The grandmother prowled around all night, was restless, noisy, disturbing and had no feeling for any of the family. Unhappily, the son-in-law was a very patient, long-suffering person. He never made any objections concerning the presence of, and the support of his mother-in-law. Mrs. F. could see that she was not discharging her duty to her husband and her children, but she could never take the step of placing her mother in a Home. After several interviews with Mrs. F. and her husband, Mrs. F. finally came to the point of saying "If only my husband would take the responsibility of saying that he wanted my mother out of the home." Eventually, however, Mrs. F. saw that this was her decision to make. If her husband took the authoritative stand which she was demanding, if she had not resolved her own conflict about the rightness of placing her mother, this might be the beginning of discord between husband and wife. It was her problem and she had to face it with some maturity.

The medical and psychiatric findings indicated that Mrs. O. needed hospitalization, preferably in a mental hospital. It was also evident that Mrs. F. could not take the complete step of placing her mother in a mental institution. Since the mother had no history of suicidal or assaultive tendencies, the medical and social staff of the Rosa Coplon Home decided that for the sake of this family, the mother would be admitted on a trial basis, thus enabling the daughter to take the first step in her own maturing process. The mother was admitted and for a very short time she seemed to be adjusting. When Mrs. O. finally became assaultive and it became impossible to keep her in the Home, the daughter was prepared to take the next step and have her mother committed to a hospital for the mentally ill.

These examples point up the change in thinking concerning the function of a Home and also the role that a case worker plays. In neither of these 2 cases was the prognosis favorable for long-time care. It was evident, however, that admission to the Home could be a therapeutic step toward the solution of the problems presented.

In less dramatic situations, the intake process offers the social worker the opportunity to lay foundations for realistic cooperation and continuing responsibility of the children for the parents after admission. Often the opportunity arises in discussing the maintenance fee. The worker gives the relatives a realistic picture of the limitations, as well as the advantages, of the Home. She points out that the Home will meet the basic needs of shelter, food and medical and nursing care, and will afford the ancillary benefits such as occupational therapy, work therapy, recreation, physiotherapy as indicated, and religious services. Nevertheless, the relatives are told, they should not expect the individual attention that the parent perhaps has received in their home or has been given in the hospital when he was acutely ill; and that our nursing staff, although adequate, is not sufficient to provide continuing special nursing for any one patient. This the social worker does, knowing full well that although the relatives say that they understand and accept the limitation—at the time they really mean it—she will need to maintain a continuing interpretive role after the admission.

Domiciliary residents

Upon admission, the reception which a new resident receives from the staff and other residents is often a crucial factor in early adjustment. After admission, the rate and degree of adjustment is different for every newcomer. What the social worker does to help, depends upon the personality and the special needs of the person involved. If his physical and mental condition is such that he is placed

in the domiciliary wing, the social worker smooths the way for him. Someone has said that the social worker acts as a "shock absorber"; better yet if she can act as a "shock preventor." To the extent feasible, proper introductions are made to fellow residents, to roommates, and to staff members who will be ministering to his needs. These staff members (nurses, the executive housekeeper and the administrator) have been previously informed concerning these needs.

The new resident is given the most necessary and immediate information concerning meal schedules and daily routine. Other information concerning the activities and the programs carried on in the Home are better imparted by slow degrees, as the occasion arises. Too often, large doses of orientation cannot be assimilated and only add to the confusion and frustration of a new resident. Above all, he must feel that the social worker recognizes his individuality and is really concerned with his particular needs and is available when he needs help. At best it takes time for the new resident to relate positively and securely to the social worker and to the Home. His rate of testing and developing new relationships goes on at a very slow tempo, as do all the other facets of his existence. No matter how skilled the worker and how receptive the client, there are areas where he must be allowed to, and can work out his own adjustment. As in each era of life and stage of growth, only the person involved can come to terms with reality and thereby climb one more rung in the ladder towards emotional maturity.

After the initial orientation process, some residents require very little casework service. They become integrated into the life of the Home, they participate in one or all of the activities according to their needs, they keep up their contacts with their friends and their families, and their relatives are not problems to the Home. If they have conflicts, they compromise with a reasonable degree of acceptance of the situation.

There are others, however—and they are not in the minority—who become a challenge to the administration. These are the residents who feel so superior to everyone that they cannot participate in any activity. There are those who are constantly being robbed, whose rooms are never the right temperature, with whom the food never agrees; those who eat too much and those who do not eat enough; those who complain to their relatives that no one is interested in them—not the doctor, the nurse, the social worker, just no one. The relatives, who are often guilt ridden, must be helped to understand the meaning of this symptomatic behavior. Obviously the social worker cannot carry on an intensive casework relationship in each situation, nor is it always necessary; but it is her responsibility to be aware of this symptomatic behavior, and to discover whether there is any real basis for the complaints or whether the resident's actions are only a means of making known his insecurity, resentment and dissatisfaction with himself. If the stresses are internal, the worker must gauge the treatability of the difficulty and she must interpret the meaning of the abnormal behavior to the family and the staff. To achieve the maximum results the social worker enlists the combined and coordinated help of all the services indicated—administrative, psychiatric, medical, nursing, physiotherapy, housekeeping and chaplaincy.

Sometimes the resident who presents the most baffling problems will respond

beyond all normal expectations, if the symptoms be properly evaluated and tenaciously treated. The following is an example:

Mrs. C. shortly after admission, was found almost asphyxiated, cowering in her closet. She was consumed by fear; she was afraid that her bed would be taken from her, that she could not find her way to the dining room which was directly across the hall, and that she would not be given any food. It was clear enough to the worker that her fears were definitely related to her reality situation in which she had lived for a long time. She had been widowed when her son was a very young child. All her affection, attention, and efforts were centered on this one child. For years after his marriage, which she had bitterly resented, she had lived alone, starving herself for various reasons. On the one hand, she was saving money to leave to her son from whom she had never emotionally separated herself. On the other hand, only by being very ill was she able to get the excessive attention from him which she so craved. She felt rejected, cut off from all satisfactions, and left adrift. His placement of her in the Home was the final proof to her that she had lived in vain.

In spite of the special attention which the social worker, the nursing staff and the physician attempted to give her, she responded only with further manifestations of fear and withdrawal. Serious consideration was being given to commitment to a hospital for the mentally ill, for fear that she would really be asphyxiated or that she would starve herself to death. Then she fell and broke her hip. This necessitated bed care and intensive nursing. She began to experience physical security, as her needs were cared for in a very personal and assuring manner. The medical and nursing staff were informed of her life history, her abnormal emotional attachment to her son, and her need for special care and attention.

Interpretation of her excessive attachment to, and demands upon her son, was given to him so that he began to understand and accept her behavior with greater equanimity and more favorable response.

Gradually she was brought to a good nutritional state. In fact she became and continues to be a voracious eater. It would seem that she is substituting the satisfactions of excessive eating for the unrequited love satisfactions which she used to demand from her long-suffering son. The physician, the physiotherapist, and the nurses prepared her for gradual participation in some of the activities in the Home. She began with occupational therapy. By the time she was able to walk again, she had lost a great many of her fears. True, she still demanded more than normal attention from her son, but gradually as she became interested in the activity and programs of the Home, she responded more normally to his longer and longer absences. It would be hard to believe that the plump, contented-looking old lady seen wheeling her roommate through the corridors was the same person as the emaciated, frightened patient of two years previously.

Infirmary patients

The patient who is admitted to the Infirmary is frequently too ill to participate in any active way in the admission process. For him it is imperative that the nursing staff accept him normally and make him physically comfortable. Indeed it is the nursing staff which can have the greater rapport and engender a feeling of security. Usually it is the relatives of such a patient that the social worker needs to help during the earlier period after the parent's admission. They need orientation toward the regulations of the Home, the visiting hours, registration, and payment of fees. Often they need help in accepting the changed character role of the parent, in interpretation of his strange behavior, in assuaging their guilt feelings which get the better of them in spite of their intellectual acceptance of the placement. Helen Lokshin expresses it well when she says, speaking of the adult child, "He needs to be reassured regarding his own grown-up-ness." It is a

very rewarding experience when a relative recognizes how she or he has been helped in this painful process of the admission and early adjustment of the parent.

In one instance in which the daughter found it most painful to place her mother in a Home, several interviews finally brought her to the point where she agreed to try the placement, since there was no other practical solution to her problem. A short time after her mother was admitted, she wrote the following note. "I am writing to tell you that I have finally become reconciled to mother's being in the Infirmary. After hearing her say "they treat me like a queen" I would have to be an awful die-hard to keep torturing myself with guilt feelings. She looks better and seems in fine spirits and I must admit she is kept so nice and clean. So, I am finding peace at last. Thank you very much for all you have done to help her become acclimated."

General

From the foregoing illustrations it can be seen that geriatric case-work is perforce a slow and limited process. One does not set one's sights for rapid or dramatic change. As in physical rehabilitation of the aged, one does not look for restoration of degenerated organs but for the preservation and the maximum use of them, so in case-work we do not look for a major change in personality. We only try to help the aged person find the touchstone which will enable him, often in spite of his personality quirks, to make the most of his opportunities in the time which he has left. Speaking of time, it is often the case-worker's greatest ally in helping the residents and their children to accept their reversal of roles and to think of old age and death as life phenomena—not as extinction but as a culmination.

In addition to working on a case-by-case basis with the relatives, the social worker in a Home for the Aged has the opportunity to educate lay committees and the Board to accept the practice and the basic principles of social work. She may help with the development of sound social policies regarding admission and discharge from the Home, and above all she should not miss the golden opportunity for keeping the Board abreast of the newest trends and services in the geriatric field, and to stimulate them to make available such services to the residents of the Home. For instance, in the three years in which professional social service has been introduced into this Home, 3 new programs have been added: a work therapy project, a group recreational project, and a day-care program. These services, once established, are invaluable resources for the social worker to use in the rehabilitation and self-fulfillment of individual residents.

The work therapy program has, without exaggeration, given at least 30 of the residents a new lease on life. During these work therapy days, the doctor's clinic is deserted. The most inveterate hypochondriacs are too busy to complain of aches and pains. In the assembly line, they relearn cooperation and a degree of consideration for their neighbors. Group therapy has roused one resident from almost catatonic lethargy to responsive participation and responsible leadership in the group. Another resident, so paranoid that she was unable to relate herself

to anyone, has gradually changed from a peripheral observer to a participant in the group singing. Without these resources, case work alone could not have effected such a degree of change.

With the creation of the 3 new ancillary services, the social worker has been given the job of supervising them and integrating them into the total program. Such services require volunteers in addition to professional workers. In a small Home the social worker is responsible for the training and the supervision of these volunteers.

To the administrator, the medical staff and the nursing staff, the social worker acts as an interpreter of the residents' needs. She becomes a mobilizer and a moderator, an amalgam; sometimes she even acts as a gadfly. On the job proper, the social worker, keeps records of her activity. In the case of those residents with whom there is an active counselling and helping relationship, there is a continuous record of the development of the situation and the treatment thereof. When the contacts are on a less intensive basis, there is periodic recording of the status, the health condition and the state of adjustment of the resident concerned.

In developing new programs, careful records are kept of the actions and interactions of committees, the purpose of this being 1) historical—to keep a record of the development and services of the agency, and 2) as a basis for later research.

In addition to the duties in the Home itself, a professional worker should bring the agency which she serves into the professional community. It is her responsibility, to the extent that it is possible to integrate her agency into the constellation of services for the aged and participate in creating a favorable social climate for the aged persons of the community.

All this may sound as if the social service set-up were the most important in the institution. It reminds me of a recent series of interviews by Clifton Fadiman with people behind the scenes at the Opera House in New York. He interviewed all the key persons in the production of the operas—the director, the designer, the electricians, the heads of the wardrobe and make-up sections, and many more. Each one told how much he had to supervise, how vast was his enterprise, how important his job. Perhaps it is necessary and salutary that each thinks his job so vital, and perhaps the opera could not go on without the contribution of each. But Clifton Fadiman did not lose sight of the goal, the entire cohesive pattern into which each of these functionaries fitted. So it is with social service in a Home for Aged. It is not in itself the most vital service, no matter how vital it is. In fact Homes have existed for many years without a social service department; many of them still do. However, where there is a social service department, it has a distinct, important function in the total aims of the Home. This function is to provide to such aged as need it, a place where their physical, emotional and spiritual needs will be recognized and cared for on an individual basis.

Moreover, the geriatric social worker, along with the members of all the helping professions, indeed along with all citizens of good will, has the responsibility to aid in making the community one in which its aged may live with comfort, dignity and pleasure.

EMOTIONAL AND PSYCHIC PROBLEMS OF INSTITUTIONALIZED GERIATRIC PATIENTS: EVALUATION OF HYDROXYZINE

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The geriatric patient at Pinehaven who is emotionally or cerebrally disturbed is viewed as a problem calling for a solution of the personality disorder as well as the somatic condition. The superficial mien which these patients present is often a cloak for a perplexed and driven personality, and is at times not particularly relevant to the underlying symptom complex of psychosomatic disturbances. One must dig deeper into their habits of thought and mood in order to reveal these latent conditions sufficiently. We use the word "sufficiently" with the purpose of pointing out that when such patients are aged, a total psychoanalytic follow-through is neither important nor advisable.

Perhaps before the days of modern chemotherapy, there might have been an excuse for spending months and years in bringing about a psychic purge in people of 70 and 80 years of age. Today, however, it is sufficient to decide that the patient might more readily be benefited by one of the available drug preparations proved by usage to be effective.

PURPOSE OF STUDY AND DESCRIPTION OF PATIENTS

Extensive clinical observations have shown that it is possible, by means of proper chemotherapeutic agents, to re-develop the patient's self and lead him to more normal behavior. The measures used for this purpose are: analeptics, hypotensive agents, tranquilizers, depressants, the anti-hallucinative drugs, the meprobamates, cerebral stimulants, and motor stimulants. However, this still leaves a large group of cerebrally and emotionally disturbed patients who either do not respond quickly or in whom the response is far too drastic, and must be counteracted by opposing chemotherapeutic measures. It was for the treatment of this group in particular that the search was made for a tranquilizer which would reduce the cerebral irritation without dissociating the patient from reality.

Patients

Many impulses arise from internal distress and manifest themselves in anti-social aberrations, and even violence in behavior. These apparent antagonisms to adjustment are often no more than defensive masks. This is paradoxically true also of many people who have lost the urge to develop any resistance to the stasis which has become their mode of life. They, too, are torn. These also need tranquility.

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This led us to the investigation of several of the ever-increasing number of drugs being presently brought to the attention of the medical profession.

The greatest number of geriatric patients needing this tranquility were in the group suffering from the milder, less serious psychosomatic disorders. True, they were rigid, anxious, full of fear, and in continuous solitude; they had lost the ability to cope with events, and had assumed antagonisms, manifested in such ordinary matters as refusal to take medication, or an adamant stand against getting out of bed. Yet these persons were not truly psychotic.

In any consideration of the psychosomatic disturbances of geriatric patients, it is particularly important to understand this fear and solitude of the aged. The particular choice of a chemotherapeutic agent may well be made on the basis of an understanding of these monstrously looming factors which face many an older invalid. Let us look at this fear and its companion, solitude. If the verities are to be found, each patient must be treated individually, and each patient won, regardless of the main showing of means and averages.

Fear is readily discernible, yet it must be differentiated from anxiety. In both fear and anxiety the reaction is either "toward fight or toward flight." Frequently, anxiety has no present concrete being, either physical or emotional. Though the term "anxiety" is often used as an equivalent of fear, anxiety more than fear is based on an association of a threat to the values of the personality of the individual—his self-esteem or security. Often this reaction to danger is not as readily discernible as fear, to the outsider or even to the patient.

This differentiation is relative, however, and the difference must be sought for elsewhere. It is not to be found in the reaction; but is rather found in the logic of the response (1).

The person in an anxiety state is apt to flee, when he should face the danger; or he may be "compulsively" foolhardy enough to fight when he should run away. Response to anxiety can be altered by various tranquilizers, often to a sufficient extent, at least, to give the physician time to provide amelioration or cure by other means. Unfortunately, when used in the treatment of fear or anxiety, some tranquilizers destroy the will and the ability to make the choice of "fight or flight" at a time when that choice becomes essential and decisive in any phase of life. Whether the reaction is to anxiety or to fear, the subject can not choose.

There is nothing so important to human beings as their relation to one another. These people have been largely deprived of such association, thus increasing their anxieties. They have thereby abnegated the social responsibility which, through the years, had paid off in personal growth and growth of personality. That, too, has increased their fear as to what they were becoming. Their pattern of behavior has lost the flexibility of mature adulthood, and they have become culture-bound on a level of the fixed rigidity of childhood.

Childishness is axiomatic in the aged, but the axiom is not necessarily true. In the rigid culture-bound concepts of right or wrong held by these people everything is either black or white, good or bad. Flexibility can be restored, however. The acceptance of the possibility that other opinions are valid, and more particularly, the acceptance of the idea that others have a right to a different opinion,

can be revived. Such an alteration is very important in making the aged person socially acceptable and societally useful. Several of our patients were so senile that they had reverted to childish instability, flitting from this to that in nearly all matters, personal and impersonal.

Fearsome anxiety in many of these older people stems from lack of societal contacts and responsibilities. They need reassurance. Thus, the assurance of the surrogate role of the nursing home as a foster-parent is rapidly embraced. This fearsome anxiety often stems from trauma—always psychologic, and at times even physical. This trauma is referable to unwantedness, made evident in family consultations about "What shall we do about mother"? One daughter says, "Hubby won't stand for her." The other son's wife says, "Don't want her around." The third has only 4 rooms, and so, "No place for her with our growing family. It is crowded as it is." Mother is hard of hearing. They say that she is getting senile. But she is not so deaf, and certainly not so dumb, that she cannot sense the resentment of those she loves because she is holding on to life so long as to cause them problems.

Almost all of our patients were troubled with fearsome anxiety. All felt or had experienced a loss of security, not only financial, but with respect to health. They had a deep fear of being uncared for in illness.

Specifications for tranquilizer

By the time we began this study, we had a fairly clear picture of what we wanted in a tranquilizer, namely, one which would bring calmness to the patient afflicted with anxiety.

We also had in mind a large group of our patients who either 1) had reached a level of improvement with analeptic therapy or reserpine which was somewhat short of what we desired, or 2) had not benefited from the varied therapy previously given. We sought a drug with which to nudge these patients into further response.

The tranquilizer selected should also be effective for a prolonged period (months) without appreciable side-effects, in order to give assurance of a reasonable permanence of results.

Some of the earlier tranquilizers induced a dissociation from reality which could be dangerous—at times, violently so. It would be important to avoid such perilous alterations in response, with due respect to the individuality of each patient.

Hydroxyzine. Among the drugs which we used, hydroxyzine (Atarax) yielded the most satisfactory therapeutic results for the purposes of our study. It should be emphasized that the place of reserpine and of chlorpromazine in the care of emotionally or mentally disturbed persons is largely established, and the use of these drugs in certain severe psychotic conditions is extremely effective, especially at the beginning of treatment. This applies also to azacyclonol in the treatment of hallucinative patients. Hydroxyzine, however, seems to be the agent of choice in patients suffering from removal disorientation, confusion, conversion hysteria and other psychoneurotic conditions occurring in old age.

Hydroxyzine is a piperazine derivative (2) with low toxicity (3). It has been used extensively in pharmacologic and clinical studies for the alleviation of anxiety and tension in adults (4–7) and children (8–10), psychogenic dermatoses (11), senile anxiety (12), and allergic manifestations (13). It is used adjunctively with narcotic preparations in pre-operative and pre-obstetrical procedures. It also seems to have some effect in preventing postoperative emesis.

METHODS AND MATERIAL

This study of hydroxyzine[1] was conducted over a period of twenty months, during which patients were treated for periods ranging from three to nine months. Initially 22 subjects were observed for three months, while 60 similar subjects were observed as controls during treatment with placebos or other tranquilizers. At the end of the three months, 40 from these control groups who had shown no significant favorable results (including 14 who had been receiving analeptics) were added to the hydroxyzine group. Replacements were made in the control groups. After six months, the control groups were discontinued, and additional patients were given hydroxyzine, until the total reached 101. (There were 9 others who received hydroxyzine for less than three months.) All but 12 of the 101 patients suffered from mental distress and were fearful, anxious, excitable, insecure, tremulous, and mildly or moderately confused or disoriented. The 12 exceptions were cases of conversion hysteria.

Hydroxyzine (Atarax) was given orally in a dosage of 25 mg. three times daily.

RESULTS

The results are summarized in Table 1.

With hydroxyzine therapy, there was no dissociation from reality and no loss of mental acuity. There was a change in the thinking processes in many instances. Concepts of right or wrong became more flexible. Soon these patients accepted the idea that other persons are entitled to opinions, and that these other opinions might be more valid than their own. Such an alteration in mental processes is most important in aiding the aged person to find his niche in his social environment.

Definite and rapid therapeutic response was noted in 54.4 per cent of the 101 patients treated; such a result was classified as "excellent." In 36 per cent a "good" response was observed, indicating that these patients did not show as much objective and subjective improvement as the "excellent" group and had to be treated longer than three months. There was a poor response in 9.6 per cent.

Thirty-nine patients had various degrees of confusion, either constant or transient. It might be fairly constant with regard to time, or it might be absent as to time, but constant with regard to some particular persons. It was only as the weeks went by that the various kinds of protective camouflage were uncovered. All of the 39 patients responded well to hydroxyzine. They showed a healthier attitude toward every-day situations, were much calmer, and mixed freely with other patients.

Forty-five patients, many with tension and anxiety, had been disoriented on admission, and had not responded to treatment previously given. In most old persons this disorientation derives from change of locale. It disappears in time, as

[1] Atarax, provided by the Medical Department of J. B. Roerig and Company (Division of Charles Pfizer & Co., Inc.).

TABLE 1

Therapeutic Response of Geriatric Patients to Hydroxyzine (Atarax)

Diagnosis	No. of Patients	Dosage of Atarax	Results			Duration of Treatment (mos.)	Side-Reaction
			Excellent	Good	Poor		
Removal disorientation.....	45	25 mg.t.i.d.	19	18	8	3	None
Confusion.....	39	orally	30	9	0	3–6	None
Conversion hysteria.....	12		6	5	1	3–6	None
Senile anxiety and tension...	5		0	4	1	4–9	None

day follows day in the same surroundings, which rapidly become familiar. "I belong in Room 527. Where is Room 527?" asks a patient who might well be right in Room 527 at the time of the question. Of these 45 patients with removal disorientation, 82 per cent improved considerably with hydroxyzine. Fourteen of these had previously failed to respond satisfactorily to analeptic therapy, and the other 31 had been receiving various other tranquilizers without effect for at least three months.

Five patients suffered from senile anxiety and marked tension. They were, however, well oriented and were not confused. They were not so readily responsive to hydroxyzine therapy as those who were disoriented or confused, even though many of the latter had a similar degree of tension and anxiety. In 4 the response was good, though the treatment had to be continued beyond the three-month period.

In some of these patients we had to adjust the initial dose of 25 mg. three times daily, because of slight drowsiness. This led us to prescribe hydroxyzine for patients with insomnia, giving the drug at 6:00 P.M., and at bedtime. The resulting relaxation led to a natural and long night's rest.

Several patients had intermittent claudication. We found that the contractions, particularly those occurring in the calf, abated and gradually disappeared with as little as 50 mg. of hydroxyzine per day.

The 12 patients with conversion hysteria improved dramatically when hydroxyzine was administered. Positive therapeutic effects were observed a few days after beginning therapy. For example, one 60-year-old patient with conversion hysteria and a Parkinson-like syndrome was rigid, and could not move his arms, legs, torso, neck, head or extremities. He could not unlock his jaws sufficiently to talk plainly, nor could he swallow more than a teaspoonful of soft food at one time. When he was given hydroxyzine, 25 mg. four times a day, he was able to move his neck after a few days of therapy, open his jaws sufficiently to make his speech understandable, and swallow adequate quantities of food. However, he still lay in bed with arms rigid against his thighs, extended straight and parallel. He could not be moved without pain or distress. Gradually, day by day, his body and limbs became more flexible and at the end of four weeks of therapy, he could sit up in bed. After ten weeks, he was able to walk and enter into social contact with other patients when he visited our recreational oasis.

DISCUSSION AND SUMMARY

One hundred and one geriatric patients with emotional disturbances were treated with hydroxyzine (Atarax) orally over a period ranging from three to nine months. There were 4 diagnostic groups: *a*) 39 cases of confusion, *b*) 12 cases of conversion hysteria, *c*) 45 cases of removal disorientation, and *d*) 5 cases of senile anxiety and tension.

Ninety-one of the 101 patients (90.4 per cent) benefited from hydroxyzine therapy; 10 patients did not respond. No serious side-reactions were noted. Several patients experienced slight drowsiness in the beginning of treatment.

All but 22 of these 101 patients had been receiving some form of tranquilizing or analeptic therapy, under our observation, for a considerable period. There had been no significant beneficial effect, or else serious side-effects had developed. The trial was thus weighted against hydroxyzine. Nevertheless, its value was attested by the low proportion of failures (only 9.6 per cent) in this previously unresponsive group of patients.

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BUCLIZINE, A NEW TRANQUILIZING AGENT

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In the search for antihistaminic drugs with greater effectiveness and low toxicity, a new family of piperazine compounds was recently synthesized (1). One of them, chemically constituted as 1-p-chlorobenzhydryl-4-p-tertiary butylbenzyl-piperazine hydrochloride, was subjected to intensive clinical investigation. Its generic name is buclizine.

Besides exhibiting relatively prolonged duration of antihistaminic activity (2), buclizine also proved to be an effective agent in controlling the nausea and vomiting of pregnancy (3–5), motion sickness (6) and labyrinthine disturbances. Many of the clinicians investigating buclizine observed that when the medication was given for other indications there was often a noticeable tranquilizing effect.

This study was undertaken to evaluate the ataraxic properties of buclizine[1] in a series of 50 agitated patients divided into 2 groups (Table 1). Group I consisted of 21 hospitalized geriatric patients with mild or severe senile agitation; and Group II, 29 patients seen in general practice who had anxiety-tension or anxiety-depression syndromes.

MATERIAL AND METHOD

Most of the 21 geriatric patients were in the Forest Hills Nursing Home. They were under custodial care for varying degrees of agitation as part of the picture of chronic brain syndrome. Excellent nursing attention and medical care permitted detailed observation of their day-to-day responses to buclizine. Removed from the trauma of everyday stresses at home and in business, these disturbed old people presented a fairly good control situation in which to assay the ataraxic properties of the new compound.

The 18 cases of anxiety-tension and the 11 cases of anxiety-depression were selected as representative of the patients with moderately severe neuroses and psychoneuroses seen in the average general practice. Their emotional reaction to the stresses of everyday life was exaggerated to the point where it interfered with effective functioning and actuated them to seek medical help. Outstanding among their symptoms were apprehension, anxiety, fear, withdrawal, heightened irritability, hypochondria and excessive worry.

When a patient was selected for buclizine therapy, all aliphatic sedatives (such as barbiturates) and tranquilizing medication were initially withdrawn for at least one week. Control urinalyses, hemograms, and renal and hepatic tests were made. After a complete personality profile had been drawn for each subject, buclizine was started in a dosage of 50 mg. three or four times daily. The dose was either doubled or halved, depending on such factors as inadequate response or annoying side-effects.

The Nursing Home patients were examined and interviewed two to three times weekly. Key nurses were assigned to make observations at different times of the day. Other members of the personnel were asked for comments from time to time. These reports were recorded and tabulated.

The ambulatory patients were seen customarily once a week. Besides a thorough physi-

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[1]Provided in the preparation, Softran, by the Stuart Co., Pasadena, California, courtesy of Joseph G. Galindo.

TABLE 1

Diagnoses

50 patients aged 39 to 92 (26 females; 24 males)

		No. of Cases
Group I a	Senile agitation, mild	12
b	Senile agitation, severe	9
Group II a	Anxiety-tension syndrome	18
b	Anxiety-depression syndrome	11
Total.....		50

cal examination, conversations on key subjects were held with each patient to determine the emotional context of their current behavior and feelings. Members of their families were also questioned in an attempt to obtain a less subjective view of their progress.

In several instances, buclizine therapy was discontinued in order to estimate effectiveness, tolerance or possible habituation. Most of the subjects, however, received the material continuously for five to fifteen weeks. Blood and urine studies were made every four to five weeks, for checks on toxicity.

RESULTS

In the geriatric group of 21 patients (aged 65 to 92), the 12 presenting the clinical picture of mild senile agitation responded best (Table 2). In 8 of the 12, the results were excellent; in 3 they were good; and in only 1 were they poor. In the patients experiencing the optimum effect, restlessness, anxiety and aimless hypermotoricity were replaced by calmness, sociability and a renewed interest in the surroundings. They began to participate in group activities, games and crafts, and were more pleasant to the staff and visiting members of the family. This improved level of interpersonal relationship was sustained as long as they received buclizine.

In the group responding moderately well, there were occasional outbursts of anger, hostility and irritability, but on the whole the result was good. Any response less satisfactory than this was regarded as poor.

However, when the level of senile agitation was considered to be severe, buclizine was not quite so efficacious. In this group of 9 patients, whose behavior disorder was characterized by assaultiveness, pathologic lying, aggressiveness, disorientation and kleptomania, only 2 showed an excellent response (with 100 mg. four times daily), 3 a good response, and 4 a poor response.

Among the ambulatory patients—a younger group, aged 39 to 63—the tranquilizing effect was best in the 18 suffering from the anxiety-tension syndrome. In 13 of the 18 there was an excellent response, in 3 a good response, and in only 2 was buclizine not effective. Besides relief of apprehension, jitters and worry, there was a decrease in somatic complaints such as palpitation, sighing, cramps, hyperhidrosis, tremor and insomnia.

The anxiety-depression group did not fare as well. Of 11 patients only 3 showed an excellent response, and 4 a good response; there were 4 failures.

In the younger groups, whenever the effect was poor with 50 mg. three times daily, the dosage was doubled to 100 mg. three times daily before treatment was abandoned. At this dosage level only 2 patients reported somnolence as a side-effect.

Buclizine was withdrawn suddenly for one week in 10 patients who were enjoying an excellent tranquilizing effect. In 9 of the 10, all previous symptoms returned within forty-eight hours and promptly disappeared on resumption of therapy. After ten to fifteen weeks of continuous administration, there was no evidence of tolerance in any of the subjects.

Six ambulatory patients voluntarily discontinued treatment when they felt no need for further help. None experienced any signs of withdrawal or habituation. After a lapse of three weeks, 3 of them had a recurrence of anxiety and requested resumption of therapy. This was done, and there was prompt control of symptoms.

In cases in which the effect was favorable, tranquilization first became evident within three to five days and reached an optimum level within a week. More rarely, full tranquilization required two or three weeks to achieve.

Side-effects

Laboratory work included urinalyses, hemograms and series of basic renal and hepatic tests. There was no significant alteration in any of these findings.

An interesting side-effect was the lowering of systolic blood pressure in 7 of 9 patients having concurrent essential hypertension. Apparently, diminution of psychic stress factors largely accounted for this hypotensive action.

TABLE 2

Results with Buclizine

	Excellent	Good	Poor
Mild senile agitation	8	3	1
Severe senile agitation	2	3	4
Anxiety-tension syndrome	13	3	2
Anxiety-depression syndrome	3	4	4
Totals	26 (52%)	13 (26%)	11 (22%)

TABLE 3

Side-effects of Buclizine

	No. of Patients
Somnolence	4
Dryness of mouth	2
Headache	2
Jittery feeling	1
Total	9

Other noteworthy side-effects (Table 3) included drowsiness (4 patients), dryness of the mouth (2 patients), headache (2 patients), and a jittery feeling (1 patient).

Two of the 4 cases of somnolence occurred in patients with anxiety-tension in whom the dosage of buclizine had been elevated to 100 mg. four times daily. The other 2 cases were in patients over 70 years of age, both receiving 50 mg. three times daily. In these instances, the drowsiness was relieved by reducing the dosage of buclizine to 25 mg. three times daily.

Dryness of the mouth was never sufficiently intense to require discontinuance of the medication. The headaches that occurred were relieved with analgesics. The single case of jitteriness was in a 45-year-old woman who faced a serious abdominal operation.

SUMMARY AND CONCLUSIONS

Among the 50 patients treated, 39 (78 per cent) showed a positive clinical response, which was excellent in 52 per cent and good in 26 per cent. The best results were noted in the 30 patients with anxiety-tension and mild senile agitation; in this group, 21 made an excellent response (70 per cent) and 6 a good response (20 per cent)—that is, a favorable effect in 90 per cent.

The results of the present study indicate that buclizine, a potent and versatile therapeutic agent, has clear-cut tranquilizing properties. It appears to be a safe and effective ataraxic agent for mild to moderate anxiety-tension states and mild senile agitation. When the factors of depressed emotional state or severe agitation enter the clinical picture, buclizine is of limited value.

With the tensions and stresses of everyday life mounting to a new high, the need for tranquilizing preparations is apparent. The absence of habituation, tolerance and toxicity makes buclizine of especial value. Its additional properties of antihistaminic, anti-emetic, anti-motion-sickness and hypotensive activity make it a unique compound in this field.

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THE MECHANISMS OF STRESS AND THE FORCES OF SENESCENCE

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INTRODUCTION

The assumption that stress is the major obligatory force in aging warrants critical review. Evaluations must be based on the distinctive status of the two processes. Thus far the mechanisms of stress have reached a level of physiologic definition, whereas those of senescence are being demarcated more slowly.

Two conclusions have general acceptance. The first is that the older body has a reduced tolerance for the unduly prolonged rigors of strain and stress. The second is that stress is not necessarily the major force in the progression of the unique characteristics of age. There is an endogenous quality to aging "not basically dependent on stress and disease" (1). In view of methods effective either in prolonging or shortening the life span, with changes not only in the senescent pattern but also in the associated incidence of chronic disease, this deduction might be considered an over-simplification; it has, however, the quality of inherent reality.

Up for general consideration is the relation of stress to the total process of aging, as well as the reverse—the influence of senescence on the dogmatic stages of stress reactions. For each of these mechanisms there are quantitative evaluations, either as chemical expressions of stress in the older body or as tolerance tests of the senescent organism subjected to unusual strains.

Certainly the alleged dominance of stress in the pacing of senescence has failed to get support. An increased amount of arterial calcium in areas subjected to more work may be interpreted as an aging phenomenon, but it is an interpretation with other possibilities. The chemical changes may be compensatory and thus protective, rather than degenerative and thereby weakening. Despite the demonstration of the tabulated steps of the general stress response (Selye), there is an individual quality, in that "what is stress to one person may be only a challenge . . . for another . . ." (2). Precise expositions of aging are limited by the fact that "there is at present no biochemical characteristic of 'oldness' in tissues or cells" (3). Obviously this limits the possibility of assessing the time-and-disease progression of senescence in terms of the physiologic quality of stress. Therefore, the conclusion that aging *per se* must be due to some or all of the combinations of stress *per se* lacks adequate support.

The reverse may be worth investigation; stress possibly may enhance survival. In a classic experiment involving caloric restriction with inevitable hunger, this type of stress was associated with a lengthening of life span in laboratory animals (4). The decreased caloric intake was identified with the longer survival, but the stress must have been a factor.

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Even personal attitudes toward the accumulative limitations of aging may be a strain in some aged persons. It is ironic that the common belief that stress is the cause of aging should lead to such an inverse view. In this manner, senescence itself has the capabilities of serving as a stress mechanism in the elderly person in whom such an attitude is assumed to be particularly deleterious as well as causative of the older body state (5).

DEFINITIONS

Stress is an established categorical pattern of a defensive process associated with general and specific pathologic conditions. It is a phylogenetically-fashioned physiologic mechanism distinguished from strain, which incites a wide variety of personal effects.

Senescence apparently is an equally specific personal development which, in particular, involves means for the *extension* of survival in time in association with a delay in the incidence of chronic diseases. It is modified by individual genetic overtones within a broad spectrum of species limitations.

Undoubtedly there are interlocking influences between the 2 factors which can occur without the sacrifice of the specific metabolic identities of either process. Some of this uncertainty will be eliminated by the accumulation of adequate criteria.

STRESS

Ingle regards stress as a "harmful state of disturbed homeostasis," with reservations based on the contrast between natural and experimental conditions. Only the extreme situation calls for an unusual degree of stress response; actually "changes in the secretory activity of the endocrine glands serve to maintain homeostasis, not to disturb it" (6). If the routine operation of such mechanisms serves as a protective device in the maintenance of the current status, it must be asked whether they could eventually produce unexpected by-products identified later as diseases.

Selye has defined stress as nonspecific systemic damage by which a catabolic impulse is initiated (7).

Have the usual definitions of stress and of strain, both of which tend to be safeguarding operations that mobilize certain resources and expend particular reserves, become confused? The concept of stress as a detriment must be differentiated from its features which promote anabolic effects, and lessen bone atrophy, nitrogen loss, and calcium elimination. Catabolic impulses seem to operate in short cycles of wave-like activity compared with the more tidal characteristics of constructive anabolic efforts. When the incidence of femoral fractures in comparable groups was studied according to body weight, it was noted that lighter individuals were more prone to fracture. The added weight was regarded as a force (or strain) which helped to resist the common tendency to impaired bone quality in older age (8). It would seem necessary to identify stress in both phases, depending upon whether the activity serves an anabolic end, or whether it is a catabolic defense mechanism trapped unawaredly in a specific pathologic form while enroute to a long-term homeostatic result.

ENDOCRINE MECHANISMS IN THE AGING BODY

There is evidence that the pituitary-adrenal mechanism responds with average expectancy, even in the very old. In a study of adrenocortical response to adrenocorticotropic hormone (ACTH) in young and old men, it was found that there may be a decrease in ACTH production with age, that the adrenocortical response is not impaired, and that "the long-term rate of ACTH output by the anterior pituitary is sufficient to maintain the gross functional integrity of the adrenal cortex" (9). In fowl, all of the types of pituitary cells undergo retrogressive changes with age, so that there is a cytologic insufficiency; but "whether the reduced pituitary of old birds is sufficient to meet maximum or even the minimum needs is still an open question" (10). In humans it has been shown that the production of gonadotropin is greater in aging women than in young ones, and that the pituitary gland in the older person can respond in virtually the same way as it did at a younger age (11). Along with this physiologic responsiveness, it has been demonstrated that hypophyseal changes are not marked in senescence (12).

In the thyroid gland, the uptake of radioisotopic iodine is decreased with age. In older men there is usually a decrease in the concentration of serum protein-bound iodine (PBI), an age-association that is not as marked in women. In men up to age 60, the mean serum PBI level ranges from 5.7 micrograms per 100 ml. to 4.6 micrograms; after that, it falls as low as 3.3 micrograms. In females up to age 60 the range is 4.5–5.0 micrograms per 100 ml.; thereafter there is a slow drop, so that by the age of 80 the mean level is 3.8 micrograms per 100 ml. (13). This is in agreement with the general view that the basal metabolic rate decreases slowly with age, and that the thyroid gland seems to have an age time-curve of reduced capacity compared with the pituitary gland (14).

The parathyroid glands have been observed to be very resistant to changes associated with aging (12).

The pancreas belongs to the group of organs having a high degree of correlation with the changes of age. Decreased glucose tolerance has been ascribed primarily to a deficiency in the ability of this gland to produce insulin. Almost 50 per cent of older people have a diabetic type of glucose tolerance curve (15).

A great deal of effort has been brought to focus on the structural and functional capacities of the adrenal cortex. Significant age-linked modifications in adrenocortical responsiveness have not been demonstrated. It seems conclusive that no feature of adrenocortical activity under ACTH stimulation, whether in degree, duration, or in metabolic or hematologic effects, has been found to be wanting under experimental conditions in older men (16). After administration of ACTH, the urinary excretion of 17-ketosteroids and corticoids is increased in both young and old but there is a greater increase of corticoids in the old than in the young (116 per cent as compared with 69 per cent increase) (17). The adrenal glands, in contrast to the thyroid, seem to belong to the category of organs with persistent survival of functions in old age. Such observations caused Kirk to conclude that there is "a practically preserved mechanism in old age for dealing with various forms of experimentally applied stress. . ." Noting the reduction in hyperreactivity to surgery on the part of many older people, he hypothesized that it is

not the hormonal conductive mechanism but possibly the somatic effectors which carry age's stigma of functional inadequacy. The crux of the situation is that "a lack of effect might be due to an inability of the organ to respond to an otherwise adequate stimulus because of age-changes in the organ." The failure of the prostate in old men to produce more acid-phosphatase under the stimulation of testosterone is evidence (11); a fall in the level from 14,400 units per ml. in young males to 4,000 units per ml. in old men is a useful measure of androgen activity (18). There may not be sufficient functioning parenchyma to produce this amount of enzyme even with the same degree of stimulation.

There is general agreement that "gonadal failure has remained the only endocrine alteration demonstrated to be characteristic of old age" (9). The ovary may be completely worn out and unable to respond to specific pituitary stimulation (19). Blumenthal indicts the gonads as being the most likely site of endocrine deficiency with advancing age. In the male, androgen excretion falls from 55 international units per twenty-four hours at age 30, to 8 units at age 80. Androgen values in the female (about a third of the male level at all ages) show the same percentage decline. Estrogen excretion in the male stays practically stable throughout life at an average level of 12 rat units per twenty-four hours. In the aging female, estrogen excretion falls sharply at age 40 and continues to drop throughout life from a high of almost 40 rat units to less than 7 rat units per twenty-four hours (11).

Three points emerge from this review of endocrinal, cytologic and functional capacities in the aging body: 1) there is a persistence of the integrity of the pituitary-adrenal mechanism; 2) there is maintenance of the functional capacity of the catabolism-mediating glands in contrast to a progressive loss of capacity in the glands with anabolic activities; and 3) there is a definite reduction in the biologic and chemical reserves by which anabolic effects can be accomplished. The result is a catabolic dominance. Determination of the properties of the endocrine glands themselves does not establish whether reservoirs of response are or are not more readily depleted in the old body. It is fair to state, however, that the constant adaptive chain of catabolic stress is "probably more influenced by atropy of tissue than by inherent involution of body tissues" (20).

In *stress* there is the dominant feature of a catabolic process combined with degrees of anabolic-neutralizing responses. In *aging* an important element is a failure of forces that constitute anabolism. This single distinction re-orients the view of the stress-due-to-aging association.

Features of stress, then, change with each stage of life, and there is a progressive reduction in certain capacities of the aging body. Despite the basic physiologic continuity of the stress mechanisms whatever the body's age, there are differences which are due to a reduction in functional capacities. Protective and preservative roles become dominant in older age. As a result the major responses to stress in the old organism are handicapped by senescent modification of the endocrine equilibrium coupled with curtailment of essential chemical and cytologic values. Results depend on the intensity, duration and character of the stressor, the frequency of its application, and individual hereditary or acquired means by which the physiologic cycle is completed. Despite the universality of the

general adaptation reaction, deviation from an average homeostatic status is a matter of the individual in some degree. Extent of damage, rate of repair, and nature of the disease, have a wide and unpredictable biologic range. No clinician could predict with exactitude the nature of an emerging clinical disorder as the result of a stress. He would do much better to know the strains under which his patient is maintaining normality. By summating personal history, family trends, and other features he might be able to draw up a table of likely occurrences. The individual, with his personal morbidity and mortality probabilities, remains essentially unpredictable.

It has been customary to regard stress as a variable, whereas the body is a substrate of constancy in which is enacted categorical metabolic changes. Somatic results of stress, however, do not always manifest themselves as expected pathologic effects, nor are they uniform from body to body. Expressions of abnormal states, some as transient as gastro-intestinal mucosal erosions and others as grave as malignant hypertension, indicate on the contrary that it is the stress mechanism that is the constant. The body under strain is the variable. If, for example, cold is used as a stressing agent, the steps of the reaction can be plotted in blood chemical and hormonal levels with reasonable exactitude; the somatic results are not as amenable to plotting. The impressed body is true first to itself and its own individual values and not to the constitutional mechanism of a method of stress adaptation which it holds in common with many other vertebrates. Furthermore, diseases of the general adaptation syndrome (a phrase implying survival) are not comparable directly to the diseases or to the total picture of aging, despite ultimate similarity to senescent forms. Undoubtedly there is much overlapping which is subject to etiologic interpretation. The diagnosis and description of a condition, such as osteoporosis, for example, is not an automatic answer to the question of its etiology. To state arbitrarily that stress in the aging body—with age as one of possibly a baker's dozen of potential mechanisms—must be *the* cause of bone atrophy can be erroneous. As another example, it has been stated that there is an accelerated incidence of the so-called diseases of stress. Adjacent to graphs showing dire ecologic effects, more often than not there will be others showing longer survival by more people than ever before. In this morbidity-mortality paradox the seeming increased incidence of stress effects has been accompanied by the attainment of greater degrees of senescence by more people. Stress contributes to an increase in certain diseases as well as to presenescent deaths, but this does not apply automatically to the entity that is senescence.

Older tissues may acquire, if not an actual storehouse of manifold immunities, at least a tolerance or even a defensive refractoriness to repeated injurious reactions. Whether the body with its particular personality can develop a resistance to its reaction to *strains* is much less likely.

SENESCENCE

Senescence has been defined in terms of growth inhibition or diversion, reproductive limitations, special metabolic patterns, maternal age, species and individual hereditary forces, physiologic summations as pathologic conditions,

and other factors. In arriving at a conclusion that it consists primarily of a gradual reduction in the potential for survival with a lessened resistance to distortions in health, Comfort (3) visualized the main phenomenon in aging as "the decline in resistance to random stresses." This definition is based on the progressive reduction in life expectancy associated with an increased likelihood of disease impairments. It encompasses the fall in responsive reserves. During stress (or under strain) death can be an abrupt event in the otherwise anticipated eventual expectancy of a normal species life-span, just as diseases from acute and unexpected sources can be a non-anticipatable interference in health at any age. Unless a common origin for the processes of stress and aging is found, there can be no method of equating the degree of the 2 types of expectancies. To maintain a going concern under repeated episodes of stress, there must be a balance between the catabolic impulses mediated by the pituitary-adrenal axis and the repair regulated within time and physical reserve limits by the anabolic hormones. Abilities to effect repair have been shown to be affected by age-qualified changes. These effects are augmented not so much by the persistent integrity of the stress mechanism as by the gradual reduction in compensating capacities. Using osteoporosis as an example again, the result of stress in bone at any age has pathologic characteristics which are similar to those seen in old age. The origins are not determinable histologically. In stress it is a result of insufficiently balanced catabolic effects of multiple origin; in aging there is a cumulative inadequacy of anabolic responses and morphologic capital means. This is just about as close as one can come to the basic differences in the 2 processes. It is fundamental to recognize that despite similar appearance of final pathologic forms, the causes, the rate of occurrence, and the nature of the responses are not the same (21).

A tabulation of the general properties of cells, the endocrine system and the central nervous system for each stage of life indicates that as cells change with age, as the anabolic endocrine systems pass their peak, as nerve tissues are modified, and as reserves fade, the older body finally outgrows its abilities to resist strain. Stress has not caused the aging, but the aged body yields eventually to its syndromes of depletion. By way of summarizing the differences:

1. Stress is episodic, strain is erratic, and senescence is continuous.
2. Stress is mediated by specific organ and tissue pathways, whereas senescence is a property of most tissues.
3. Stress is a short-term process with reversible qualities, whereas constitutional senescence seems to be irrevocable.
4. Stress is quantitative and predictable; aging, as yet, is a qualitative mechanism with a wide range of expression in the species.
5. Stress is revealed in certain individual disease expressions, whereas senescence remains unfractionated in its pathologic associations.
6. Stress is a defensive method which serves the potentials of senescence, whereas the aging process is a reflection of the life characteristics of the organism, including its properties for survival.
7. Stress is a catabolic state involving anti-anabolic as well as catabolic forces; the catabolic dominance in senescence is due primarily to anabolic failure.

CONCLUSIONS

The patterns of stress are not equivalent to the totality that is senescence. The forces of senescence have specific lineaments, just as the mechanisms of stress have particular characteristics. It need not follow that since similarities are strong, they must necessarily be of kin. This could be a biologic trap as well as an unwarranted conclusion. Occasionally the 2 processes abet each other, but more often than not they tend to offset themselves. If all stress stimuli could produce constant degrees of senescence, the latter would have to appear in identical degree in all persons. In the light of final pathologic expressions, this does not happen.

Stress reactions in the adequate body consist of defensive contributions to effective survival, so that an organism accumulating methods of resistance probably adds to, rather than detracts from the life span. Failures are represented by particular diseases or by premature terminations of life which are not "senescent." Stress agencies are intact during average life spans up to very old age, but the physical reserves for speedy enactment in terms of rate and quantity of metabolic change become impaired. Strain is a personal response which does not have the phylogenetic precision of the stress triptych.

Aging is a multiple phenomenon, some phases of which can be influenced by the nature, duration and intensity of stresses. Its total machinery, however, encompasses the several apparatuses of stress, at least until compensations fail. Paraphrased, the process is willing but the body reserves are weak.

There are many mutual features. Both are preservative and defensive metabolic states, changing independently of each other through the years. The nature of each reflects the full load of hereditary influences. Part of each other's effects can be read in the final pathologic result. Even in this it cannot be said that common senescent changes in the aging body are synonymous with those due to stress, even if the latter is repudiated less readily by the older frame. Increasing numbers of pathologic conditions are the evidence and the sum of the occasional failure of the old body to heal insults from its earlier years superimposed on lessened resistance in a possibly less effective old age. There is the additional fact that in a longer life, exposure to unchanging stimuli by a changing body is a common occurrence. The body and its buffering of strain may change, but the stressing agency does not.

In a sense, the expositions of the endocrine mediators of stress have diverted (for a time) the full exploitation of physiologic study of the total means by which an aging body successfully meets an amazing aggregation of hazards in a variety of calendar seasons. The continual response to stress may contribute to survival by stimulating the production and storage of antibodies, by memory of defensive tactics, by protective conditioning, by muscle training in the skill of artful dodging, and by acquired skills and learning which permit of a measure of surety in situations which formerly required the entire gamut of protective body devices. Many old bodies sustain successful survival, whereas many younger persons succumb due to failure to be versed in methods of meeting situations. It is only in the last stages that the means of meeting repeated stresses are worn away;

the old body, having used up its protective reserves, finally gives up the ghost to the last stress.

Even though stress as a catabolic force might influence the *rate* of senescence, it is doubtful whether it has a dominant effect on the *nature* of the ultimate form. In fact, there is doubt whether there is any difference in the way the old body responds to stress. The nature of stress syndromes can be a part of the whole picture of everything that happens during survival and in aging, without requiring the inference that stress is the cause of senescence. Stress clocks the time necessary to mobilize forces of response, if such reserves are still available, but it does not designate the total, often individualized, procedures involved in senescence.

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BENZILIC ACID DIETHYLAMINOETHYLESTER HYDROCHLORIDE (PHOBEX) IN THE TREATMENT OF CHRONICALLY PSYCHOTIC PATIENTS

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Benzilic acid diethylaminoethylester hydrochloride (Phobex) is a peripheral anticholinergic agent. It also acts centrally (1), and because of its normalizing effect on mood, may be called an antiphobic drug. It increases the emotional threshold for external influences in many cases of chronic psychosis. When used in normal subjects, alterations in autonomic mechanisms following verbal stimulus are more pronounced than in psychoneurotic patients. However, there is a tendency towards inactivation following repetition of the stimulus in normal subjects, whereas the reaction is provoked with the same intensity by repetition of the stimulus in psychoneurosis (2). Intellectual functions, as measured by association, abstraction and similar tests, are not altered by Phobex (2), making it advantageous for use in workers requiring full intellectual control.

CLINICAL MATERIAL AND METHODS

Our study, undertaken in June 1956, involved 2 trials of Phobex in 2 groups of female patients with chronic psychoses. In Group 1 there were 60 schizophrenic, senile and arteriosclerotic patients. Many of them were tense and nervous under stress from their delusions and hallucinations which, in turn, were produced by their inner conflicts. In Group 2 there were 57 schizophrenic, senile, arteriosclerotic and manic-depressive patients. However, Group 2 included 37 of the 60 patients in Group 1 who had been taking Phobex for two months or less.

The dosage of Phobex ranged from 1 mg. to 10 mg. three times daily, by mouth. The initial dosage was usually 2 mg. three times daily. This was increased or decreased according to the reaction of the patient. In the cases of depression it was used in combination with such drugs as meprobamate, perphenazine or chlorpromazine. Psychotic patients require much larger doses of neuroleptic drugs than do psychoneurotic patients. A dosage of 0.5–1.0 mg. three times daily was considered sufficient for psychoneurotics in one study by Jensen (3).

RESULTS

The results of therapy are outlined in Table 1.

In some instances the beneficial results could be noted three or four days after Phobex was started; in other instances, improvement was noted only after an increase in the dosage.

In the first trial with 60 patients who took Phobex for periods ranging from five weeks to six months, 18 per cent were considerably improved, 30 per cent were slightly improved, and 52 per cent showed no change. No side-reactions occurred.

In the second trial with 57 patients who took Phobex for periods of from one to twenty-three months, 2 per cent were greatly improved, 24 per cent were

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TABLE 1

Clinical Results of 2 Trials with Phobex

	Group 1	Group 2
Number of patients	60	57
Types of patients	Schizophrenic, Arteriosclerotic, Senile	Schizophrenic, Arteriosclerotic, Senile, Manic depressive
Daily dose of Phobex	3 to 30 mg.	3 to 45 mg.
Average	15 mg.	20 mg.
Duration of therapy	5 wks. to 6 mo.	1 to 23 mos.
Side-reactions	None	Depersonalization, Dizziness } 5%
No change	52%	38%
Improved	48%	62%

considerably improved, 35 per cent were slightly improved, and 38 per cent showed no change. The increased percentage of improvement compared with the first trial was associated with increased dosage of the drug. Side-reactions occurred in 5 per cent of the second group. These reactions consisted of dizziness and a sense of depersonalization, and were alleviated by reduction of dosage or stopping the medication.

CONCLUSION

Phobex is a useful drug in the treatment of chronically psychotic patients, including those who are senile or arteriosclerotic. Side-effects are minimal.

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Abstracts of Current Literature

COMPARISON OF OVARIAN AND ENDOMETRIAL MORPHOLOGY SPANNING THE MENOPAUSE.

Bigelow, B. *Obst. & Gynec.* **11:** 487 (May) 1958.

Endometrial morphology and ovarian morphology have been studied and compared in 300 consecutively selected patients treated only by hysterectomy and salpingo-oophorectomy. The cases form 4 clinical categories spanning the menopause and are composed of the following age groups: 100 aged 45 to 49; 100 aged 50 to 54; 100 aged 55 and over. Evidence is reviewed that functional relations between endometrium and ovary persist into the postmenopausal state. Eleven morphologic categories for evaluating endometrial activity are described. They range from normal activity to inactive on the one hand and carcinoma on the other. With increasing interval beyond the menopause, inactive endometria rose in incidence, but were infrequent compared to hyperplastic, anaplastic, or carcinomatous endometria. Hyperplasia and anaplasia or carcinoma *in situ* reached peak incidence four to nine years postmenopausally. True invasive carcinoma, however, rose progressively to peak incidence 10+ years postmenopausally. The morphologic criteria for evaluating alterations of ovarian cortical stroma are described. With the occurrence of the menopause, and thereafter, the ovaries showed loss of cystic follicular derivatives and increasing alterations of the cortical stroma—more diffuse hyperplasia, better defined cortical thecomatosis, and cortical granulomata. Cortical stromal fibrosis had no rising incidence parallel to that of stromal hyperplasia. Cortical thecomatosis had a more significant association with stromal hyperplasia than did cortical granulomata or cortical stromal fibrosis. In the premenopausal group, significant correlation was found between the presence of luteinized cystic follicular derivatives in the ovaries and abnormal endometrial activity. In the menopausal and postmenopausal groups, no significant correlation was found between alterations in ovarian cortical stroma and degree of endometrial activity. (From author's summary.)

PRIMARY OR IDIOPATHIC DIABETES INSIPIDUS: A SYSTEM DISEASE.

Blotner, H. *Metabolism* **7:** 191 (May) 1958.

A study of the pathologic changes in true idiopathic diabetes insipidus is presented, with postmortem reports on 3 cases. The findings support a new concept, that idiopathic diabetes insipidus is a system disease due to primary degeneration of the supraopticohypophyseal system without obvious reason. Why the degeneration is limited to this area is unknown. In 2 of these cases, marked loss of nerve cells in the supraoptic nuclei, which contained hardly any characteristic nerve cells, and a considerable degree of localized astrocytic proliferation in the same region were noted. The paraventricular nuclei likewise showed some cell loss, although to a lesser degree than the supraoptic nuclei. The supraoptic nuclei in the third case were not studied. The posterior lobe of the pituitary gland was normal on routine microscopic examination in all cases, although somewhat reduced in size. However, no neurosecretory granules were noted in the posterior lobe in the case studied with Gomori's stain. An etiologic classification of 124 cases of diabetes insipidus is presented. (From author's summary.)

THE POSTURAL DENSITY CHANGE OF URINE IN THE DIAGNOSIS OF EARLY CIRCULATORY FAILURE.

Burdon, J. F. *Practitioner* **181:** 81 (July) 1958.

A new specific-gravity comparison test can detect fluid retention and subsequent nocturnal polyuria before postural edema becomes evident clinically. Such conditions as cardiac failure, hypertension, anemia, toxemia of pregnancy, and myxedema can be de-

tected by this test because they produce insidious daily fluid retention, and this fluid is expelled due to circulatory improvement when lying down at night. The test is based upon the changed specific-gravity pattern. The tissues can conceal approximately a liter of water in excess of their requirements without evident edema, but this amount of water added to the night urine will dilute it to one-third its normal volume. Also, if this water is withheld from the daily urine, it will concentrate to about one-third, so that the ratio between the night and day strengths will be strongly affected by even small amounts of water retained by day and expelled at night. For this test, the patient is asked to drink nothing after 5 P.M. (If he is unusually thirsty, he must report what he drinks.) The first urine specimen in the morning is added to the urine passed during the night. The second specimen is collected three hours later. The specific gravity of each is determined with a urinometer. The difference found by subtracting the second value from the first represents the "postural density change index." It indicates the degree of nocturnal concentration and is approximately +10 in normal persons. The index was tested in healthy subjects with normal consumption of fluid in the evening. Under these circumstances, the average value was +8; the index was never negative. In renal failure, the index approaches zero as the concentrating power of the kidneys fails. In circulatory failure, with its reversal of specific-gravity pattern, a negative index is found, which is the earliest sign. In this test, no negative index is accepted unless it has been determined following fluid restriction. Case reports for conditions producing a negative index are given as follows: myocardial weakness, vascular incompetence, hypertension, myxedema, varicose veins, and obesity. No case reports are included, but this test should also prove useful in toxemia of pregnancy, anemia, nutritional deficiency states causing edema, and in the discovery of diabetes and uremia in obscure illnesses.

THE ROLE OF PSYCHIATRY IN THE TREATMENT OF PARKINSON'S DISEASE.
Chafetz, M. E. *Geriatrics* **13:** 435 (July) 1958.

Successful treatment of Parkinson's disease requires an approach that considers the patient from an emotional as well as a neurologic point of view. It is recognized that emotional and stressful factors intensify the symptoms. In addition, different personalities react to the threat of the disease in special ways. This variation in response must be dealt with if maximum therapeutic benefit is to be achieved. Some patients will have had a psychiatric disorder before the development of parkinsonism. In others a profound reactive depression develops in the presence of a chronic disabling disease. This is more likely to happen in geriatric patients. Others suffer from psychotic-like states as a result of drug-induced sensitivity reaction to belladonna drugs. Still others have a personality structure that makes them unable to adjust to the limitations imposed by the disease. A patient may respond to gradual onset of the disease by seeking the cause through medical examination, but he may respond by denying it and substituting some other means of carrying out a motor activity until such time as his obvious impairment makes diagnosis and treatment mandatory. The sudden onset of Parkinson's disease may be associated with some sudden, severe emotional trauma. Once a patient learns the diagnosis, he is likely to react with hopelessness and the thought that he soon will reach a completely helpless state. The patient who has the most difficulty in adjusting to his state is one with an obsessive-compulsive personality structure who becomes frustrated because he cannot deny the disease and function independently as before. As a result, he suffers an increase in symptoms. As the emotional disturbance is heightened, this type of patient is likely to "freeze" and become unable to perform a single motor act because of his terror. Emotional factors operate at both conscious and unconscious levels, so that a pattern of uneven responses is produced. As a result, the patient's family is likely to think that he sometimes is not trying as hard as he might. This increases tension and creates a more difficult life situation because attention is focused on the patient. Because he can no longer maintain his "perfect" approach to life, because of his bizarre symptoms, and because of his underlying psychologic conflict,

he frequently becomes dependent upon the physician and upon medicines. The loss of social contact and gratification from his environment increases his depression and intensifies the symptomatology. The psychiatric treatment of Parkinson's disease requires a healthy physician-patient relationship wherein the patient feels free to ask trivial questions and express his fears, and the physician responds with kindness and understanding. In addition, the physician needs to take the time to understand the patient's work, and his social and family settings in order to help him arrange his life activities within the limitations of his disease. A specific treatment regimen time-ordered for the compulsive patient helps him to re-establish a successful psychologic defense mechanism. The physician must also help the family to understand the disease in order to eliminate unnecessary stresses for the patient. The necessity to maintain social contacts is paramount. When the emotional disturbance is profound, the services of a psychiatrist should be sought. Group therapy has helped patients overcome their self-imposed isolation, and has given them a chance to express their fears and derive reassurance from fellow sufferers. It has shown how denial operated in these patients. This mechanism could not operate completely because of the presence of actual disease, so that varying degrees of depression were present. This could be dispelled by the support and assurance derived from the group structure, from aid given by one patient to another, and from active participation of the group leader. The fact that the latter answered technical questions repeatedly in a calm manner gave the patients confidence because it clarified misconceptions and showed that the physicians were not afraid to talk about the future of the disease. If the parkinsonian patient is helped to face and examine his individual needs and fears, it is thought that he may learn to adjust to a chronic infirmity and derive a gratification from life that he otherwise would not have.

SURGICAL TREATMENT OF MASSIVE UPPER GASTROINTESTINAL HEMORRHAGE. Cooper, D. R.; Stahlgren, L. H.; Sylvester, L. E., and Ferguson, L. K. *Gastroenterology* **34:** 947 (June) 1958.

Problems in the management of patients with massive upper gastro-intestinal hemorrhage remain unsolved. A plan to separate probable fatal bleeders from those who probably will recover with conservative therapy includes: 1) determining whether the bleeding is massive, by observing the patient's response to the hemorrhage and replacement therapy; 2) determining whether the bleeding point is located in the upper gastro-intestinal tract; for practical purposes this is established by the presence of hematemesis, bloody gastric aspirate, or positive results with the Einhorn string test; 3) excluding the presence of esophageal varices by a careful history and physical examination, a bromsulphalein test, and barium study or endoscopy as indicated; and 4) learning whether there is any evidence of a bleeding tendency. Barium x-ray examination of the stomach and duodenum during the bleeding is not considered necessary. Once it is established that the lesion is located in the stomach or duodenum, that is, is accessible to abdominal operation should that prove necessary, therapy consists of adequate transfusions, strict ulcer diet, and sedation. A decision to operate is reached only after it is determined that the hemorrhage will not cease with this regimen. The criteria for operation are exsanguinating hemorrhage, continued bleeding requiring replacement of more than 500 cc. of blood every eight hours for forty-eight hours, and rebleeding while the patient is hospitalized and receiving antiulcer treatment. The exact source of bleeding usually can be determined at laparotomy and should be excised. If there is great risk to contiguous structures, simple ligature about the bleeding point may be performed. If no lesion is apparent upon external inspection and palpation of the viscera, a blind gastric resection may be performed, being careful to carry the resection high on the lesser curvature, with reasonable assurance that the bleeding point will be controlled. Gastrostomy and duodenotomy are reserved for instances in which the bleeding point cannot be localized to the stomach or duodenum, or in which temporary control of profuse bleeding is necessary while gastric resection is performed. Emergency gastrectomy performed in these patients will carry a higher mortality rate than the elective procedure

because of the precarious state of these acutely bleeding and depleted patients. Experience with this plan in 46 patients who underwent gastric resection for massive upper gastro-intestinal hemorrhage is reviewed. Half of the patients were between the ages of 50 and 70 years and 39 per cent above age 60 years. Despite the fact that all had severe bleeding with poor prognoses, an 81 per cent survival rate was obtained. The 19 per cent mortality rate occurred because operation was performed in many instances as a last resort with little chance of success. It was possible to control bleeding by operation in 96 per cent of the patients. Extreme old age adds to the surgical risk because these patients tolerate anoxia and shock poorly. In them, early operation is essential. If the optimum time for operation is lost, then conservative treatment must be adhered to strictly. In elderly patients, simple ligation or segmental resection may be of value if the bleeding point cannot be located. It is concluded that the mortality rate in massive gastro-intestinal hemorrhage can be lowered chiefly by an early decision for or against surgical intervention. Some patients will be salvaged by operation who would become exsanguinated under conservative management.

CLINICAL PATTERNS OF PEPTIC ULCER AFTER SIXTY.

Cutler, C. W., Jr. *Surg., Gynec. & Obst.* **107:** 23 (July) 1958.

Among 3,049 patients with peptic ulcer seen in a 16-year period, 430 patients were over 60 years of age. The average age was 66.4 years, and the oldest patient was aged 89. The ulcer locations were as follows: duodenal, 286; gastric, 126; duodenal and gastric, 8; marginal 10. Other conditions that affected treatment were cardiovascular disease, prostatism, cholecystitis, anemia, chronic bronchitis and emphysema, carcinoma, kidney lesions, obesity, cirrhosis, arthritis, diabetes, and Parkinson's disease. The following observations were made in a study of these elderly persons with peptic ulcer. The duration of symptoms was much longer than in younger age groups. Few of the ulcers developed for the first time after age 60. When they did, they were often manifested by severe hemorrhage or by perforation, either without symptoms or with symptoms of short duration. Hemorrhage was the most frequent of late complications that created an emergency. In a sizable proportion of the cases, bleeding had previously occurred periodically. The cases in which it was the first symptom after age 60 were likely to be severe and dangerous. Next most frequent of emergency situations was perforation of the stomach or duodenum. This usually occurred in the older cases rather than in ulceration more recently developed. Obstruction, a less acute emergency, could not long be tolerated by these elderly patients. Patients with obstruction almost invariably had ulcers of long duration. Intractability was the reason for hospital admission of 207 of the ulcer patients. In many cases of hemorrhage, especially when it was massive or recurrent, surgical management became mandatory. When the circumstances warranted it, partial gastrectomy proved to be safer than letting the bleeding continue. The outcome was successful in most of the patients in whom it was undertaken. Surgery also was mandatory in cases of perforation of the stomach or duodenum. In these elderly patients, simple closure of the perforation proved the safest procedure. In cases of obstruction or intractability, unless the patient's status was good and there was reasonable assurance of the safety of partial gastrectomy, it usually proved wise to perform a less hazardous procedure. This was not done, however, when carcinoma was suspected. In all types of complication except perforation and massive, continuing, or recurrent hemorrhage, medical therapy was well warranted. The impression gained from this study was that the many factors modifying the situation in the elderly peptic ulcer patient makes it necessary that each case be considered a distinct problem.

CLEARING FACTOR INHIBITOR IN HUMAN ATHEROSCLEROSIS.

Day, A. J., and Wilkinson, G. N. *Circulation* **18:** 76 (July) 1958.

The inhibitor effect of the plasma of atherosclerotic, diabetic, and nephrotic patients on the *in vitro* clearing activity of post-heparin plasma was determined and compared with that of student controls and older controls. A significant increase in inhibitor activity was

shown to exist between the older control group and the student group. A similar increase in inhibitor activity was demonstrated when the atherosclerotic group was compared with the student group, but no difference existed when compared with the control group of similar age. An increase in inhibitor activity was found in both the diabetic and nephrotic groups, but again no difference when the age effect was eliminated. It was considered that an increased level of clearing-factor inhibitor results from aging, but that no increased activity occurs with atherosclerosis, diabetes, or nephrosis, other than that accounted for by age. (From authors' summary.)

GASTRIC CANCER AND ATHEROSCLEROSIS.

Dungal, N., and Benediktsson, T. *Lancet* **1:** 931 (May 3) 1958.

A study was made in Iceland of a possible relationship between gastric cancer and atherosclerosis. In that country, gastric cancer is common, but arteriosclerosis is less prevalent than in other countries. Among 1033 necropsies of people aged 50 years or over, 104 gastric carcinomas were found. The condition of the aorta of patients with gastric cancer was compared with that of control patients of the same age without carcinoma, and with that of patients with gastric ulcer. The results were as follows: In gastric cancer, the incidence of atheromatosis was 32.3 per cent and of calcification of the aorta 26 per cent. The percentages, respectively, in the control patients were 31.3 and 47.3 per cent, and in those with gastric ulcer 27 and 51.4 per cent. A higher rate of calcification was found in women than in men. This finding may have some significance in view of the higher incidence of gastric cancer in men. The experience gained in this study tends to confirm that old people with smooth aortas are more likely to contract gastric cancer than are those with greater intimal changes. No explanation is offered for this apparent causal relationship.

DIRECT SURGICAL RELIEF OF CORONARY ARTERY OCCLUSION.

Gottesman, L. *Am. J. Cardiol.* **2:** 315 (Sept.) 1958.

Efforts to relieve myocardial ischemia directly by surgery are reviewed. For some time past, the surgical approach has been devoted to developing new channels for blood supply to the myocardium. Recently, however, the concept of selective potential of the surface of the heart and its relation to ventricular fibrillation has gained attention. Experiments in dogs indicate that direct surgical relief of obstructive coronary atherosclerosis may be possible. This may be accomplished through the use of coronary thromboendarterectomy or of an arterial bypass to restore blood flow. A few successful operations with these technics in human beings have been reported. However, criteria for the selection of suitable patients have not been established. Before these technics can be employed, coronary angiography will be required in order accurately to diagnose coronary artery obstruction.

A NEW NEEDLE AND SAFER METHOD OF ARTERIOGRAPHY.

Husni, E. A. *Surg., Gynec. & Obst.* **106:** 627 (May) 1958.

A new needle for arteriography reduces the likelihood of some of the serious complications of this procedure. The needle has a solid tip with a short, sharp bevel and a side aperture. Its advantages over standard needles are as follows: 1) Bleeding from the puncture site is lessened. 2) The needle is unlikely to punch out a piece of arterial wall which may act as an embolism. 3) The possibility of extraluminal and intramural injections of contrast medium is nullified. The side aperture will not allow back bleeding unless it is within the lumen of the vessel. The aperture contains a sector that acts as an atomizer so that contrast medium is delivered as a spray. The immediate distance affected by the spray is one-third that affected when a standard needle is used. The dilution of injected contrast medium takes place rapidly. The side-opening permits control of the direction of injection of the medium. A safer method of arteriography makes use of local procaine rather than general anesthesia. An intra-arterial test dose of 1 cc. of contrast medium (iodopyracet) serves as a

sensitivity test in addition to that provided by an intradermal skin test. This test dose allows a check to be made of the position of the needle in abdominal aortography, so that it can be reinserted if desired. The quantities of 35 per cent iodopyracet usually suitable for femoral arteriography have been 15 to 25 cc., and for abdominal aortography 20 to 25 cc. of 70 per cent iodopyracet. The radiologist is protected from unnecessary radiation by the use of a long piece of plastic tubing between the syringe and the needle, which permits him to stand behind a lead screen.

SUBACUTE HEPATIC NECROSIS AND POSTNECROTIC CIRRHOSIS DUE TO ANICTERIC INFECTIONS WITH THE HEPATITIS VIRUS.

Klatskin, G. *Am. J. Med.* **25:** 333 (Sept.) 1958.

Nine cases of subacute hepatic necrosis with progression to postnecrotic cirrhosis are described, in which the disease appeared to have its inception in an attack of anicteric viral hepatitis. In each instance biopsy material was obtained sufficiently early in the course of the disease to demonstrate the histologic features usually considered diagnostic of the infection. With 1 exception, all the patients were middle-aged or elderly women. Characteristically, the onset was relatively abrupt, with nonspecific constitutional and gastrointestinal complaints, but was followed within a period of two to eighteen months by the appearance of frank signs of chronic liver disease. Jaundice was a late development in 8 of the 9 cases, becoming evident in three to fifty-five months from the onset. Often it was accompanied by dark urine, light stools, pruritus and hyperphosphatasemia, features that frequently were misinterpreted as evidence of extrahepatic biliary obstruction. In addition to the hyperphosphatasemia, marked hyperglobulinemia and high levels of thymol turbidity were helpful diagnostic clues. The disease tended to run an intermittently progressive course that was little affected by dietary measures and bed rest, and terminated fatally in 5 of the 9 cases. Evidence is reviewed to show that females at all ages are peculiarly susceptible to the anicteric form of viral hepatitis that produces subacute hepatic necrosis and postnecrotic cirrhosis. The suggestion is made that such infections, which are readily overlooked or misinterpreted, may account for many instances of otherwise unexplained cirrhosis, and particularly those of the classic postnecrotic variety that occur in females. (From author's summary.)

MASKED DEPRESSION IN MIDDLE AGED MEN.

Kral, V. A. *Canad. M. A. J.* **79:** 1 (July 1) 1958.

When an apparently neurotic reaction does not clear with the use of psychotherapy alone or in combination with drug treatment, the possibility of a masked depression should be considered. The presence of signs of autonomic disturbance and a low sedation threshold would favor such a diagnosis. Five cases of masked depression in middle-aged men are presented. All had previously shown neurotic trends. The depression in each was precipitated by a traumatizing event. At first these patients appeared to have a neurotic anxiety reaction. A depressive mood and psychomotor retardation were minimal. All had autonomic disturbances—anorexia, insomnia, weight loss, and impotence. Electroencephalographic examination showed that each had a low sedation threshold. The anxiety reaction responded only in part and temporarily to psychotherapy, somnolent insulin, and tranquilizing drugs. As the anxiety and tension lessened, the underlying depression became apparent. This responded favorably to electroconvulsive treatment, which is the one of choice.

LONG-TERM OR MAINTENANCE ADRENAL STEROID THERAPY IN NONTROPICAL SPRUE.

Lepore, M. J. *Am. J. Med.* **25:** 381 (Sept.) 1958.

Experience with long-term, low-dosage maintenance therapy with adrenal steroids given orally to patients with intractable nontropical sprue has established that this is a

more feasible method of treatment than is short-term therapy. Its use should be reserved, however, for patients with intractable sprue who have failed to respond to standard measures consisting of the administration of special diets, vitamins, folic acid, and vitamin B_{12} or liver extract, and who have had a trial of a gluten-free diet. It should be avoided in patients suspected of having active tuberculosis and in those with emotional instability. The case reports for 6 patients who responded well are presented. They demonstrate that relapses occur within a few weeks when intermittent therapy is used, whereas patients under long-term therapy are likely to remain in good health. The dosage required for maintenance, has not exceeded 50 mg. of cortisone, 40 mg. of hydrocortisone, or 10 mg. of prednisone, and usually has been lower. Despite the continuous use of steroids in these 6 patients for one to six years, no complications have occurred. An instance of reactivation of tuberculosis in a patient who failed to respond to steroid therapy is reported. The mechanism of action of adrenal steroids in sprue is still obscure despite many attempts at explanation. It would appear that they in some unknown manner influence the absorption of various substances from the small intestine.

DISSECTING ANEURYSM OF THE AORTA: A NEW SURGICAL PROBLEM.
McBurney, R. P., and Rodda, T. S. *Am. Surgeon* **24:** 381 (May) 1958.

Recent advances in the surgical treatment of dissecting aneurysm of the aorta change it to a practical problem. If the diagnosis can be established early and treatment instituted promptly, there should be an excellent chance of lowering the previous mortality rate of 80 to 90 per cent. The clinical features of dissecting aneurysm of the aorta were determined from a review of 13 cases on which necropsy was performed. The incidence is highest in the fifth, sixth and seventh decades, and men predominate by about 2.5 to 1. The outstanding complaint is pain. If the thoracic aorta is the original site of dissection, the pain occurs in the chest and upper back. It may go into the neck, head, jaw, or arms if the innominate, carotid or subclavian vessels are involved. As the dissection progresses, the pain moves down the back and chest to the abdomen or low back, and may radiate into the legs. The onset of pain is sudden, knifelike, and incompletely relieved by narcotics. An episode of syncope may sometimes be the initial symptom. The physical signs of pallor, cold clammy skin, elevated pulse and dyspnea are the most common. A check should be made for signs of arterial occlusion in the distal arteries. The presence of elevated blood pressure in the upper extremities with low blood pressure in the lower extremities is suggestive of the diagnosis, as is the presence of hypertension with signs of shock and of an aortic diastolic murmur. Miscellaneous findings may be a pulsating abdominal mass or signs of chest fluid or cardiac tamponade. There may be anemia consistent with loss of blood and elevation of the non-protein nitrogen level. The most common pattern for the electrocardiogram is that of left-heart hypertrophy and strain; it is exceptional for it to show findings typical of coronary occlusion. In the series examined, the chest roentgenogram in approximately half of the patients showed a widened aortic shadow. An angiocardiogram may prove helpful. The differential diagnosis usually is among coronary occlusion, ruptured aneurysm, mesenteric thrombosis, acute pancreatitis, and pulmonary embolism. Dissecting aneurysm of the aorta is a surgical emergency. The most successful surgical procedures appear to have been a fenestration type of operation, excision with grafting in cases in which dissection begins below the left carotid, lateral aortorrhaphy, and division of the aorta and production of a re-entry site for the dissection.

SOCIAL FACTORS IN OLD AGE PSYCHIATRY.
Post, F. *Geriatrics* **13:** 576 (Sept.) 1958.

This review examines and evaluates evidence suggesting that psychologic disturbances in elderly persons may have social causes at the level of culture, society, work situation, and family. Little evidence has been discovered to show that psychiatric disorders in elderly persons are caused by the impact of the society in which the person lives, although the

effects of the disorders may be aggravated or relieved by social factors and social action. It is more likely that etiologic factors in the old person's immediate social environment at his work and within his family are of greater importance. Approximately one-third of elderly people requiring psychiatric treatment show no intellectual impairment but suffer from so-called functional psychiatric syndromes. Neurotic disturbances exceed in frequency and social significance the so-called mental illnesses among them. Some success has been achieved with socio-occupational therapy planned to increase the number of communications between demented old people and their environment. Their dementia has not been lessened nor retarded, but the encouraging results make this kind of therapy a possibility in less deteriorated old people living in a community. Although the evidence for social causes of psychiatric disorders in elderly persons is fragmentary and often contradictory, it is suggested that carefully controlled therapeutic trials of social measures be carried out.

DIAGNOSTIC VALUE OF SERUM TRANSAMINASE ACTIVITY IN HEPATIC AND GASTROINTESTINAL DISEASES.

Pryse-Davies, J., and Wilkinson, J. H. *Lancet* **1:** 1249 (June 14) 1958.

The application of temperature corrections improved the precision and sensitivity of spectrophotometric determinations of serum glutamic oxaloacetic transaminase (SGOT) and glutamic pyruvic transaminase (SGPT). Studies of the SGOT and SGPT activities in 50 healthy subjects aged 19 to 50 years, and in 127 patients with no hepatic or cardiac disease, established that values above 40 SGOT units per ml. and 30 SGPT units per ml. (corrected to 25°C.) should be considered abnormal. These activities were then determined in acute hepatitis, obstructive jaundice, cirrhosis and chronic hepatitis, liver metastases, ulcerative colitis, toxic hepatitis, liver infarction, and partial hepatectomy. High values (above 500 units) of SGOT and SGPT were found to be characteristic of infectious hepatitis. High values also have been reported in carbon tetrachloride poisoning. In this study, high values were found in the sera of rabbits treated with carbon tetrachloride but no measurements were made on human beings. Only in these 2 conditions are these determinations reliable when used alone. In conjunction with other liver function tests, however, they are useful in the detection of liver diseases, some of which may otherwise remain undiagnosed. Values of 100 to 300 units per ml. were found in obstructive jaundice, glandular fever hepatitis, and toxic hepatitis (exclusive of that due to carbon tetrachloride). Determination of these activities is of less diagnostic value in cirrhosis and cases of metastases of carcinoma to the liver. The SGOT level was above normal in 64 per cent of the patients examined, whereas the SGPT level was raised in only 40 per cent of patients with these diseases. The value of SGPT determinations was illustrated in a case of suspected myocardial infarction. Elevations and fluctuations in the SGOT level were paralleled by changes in the SGPT level, suggesting that the liver and not the heart was the source of the SGOT. The patient actually had cholelithiasis and the elevated transaminase activity probably was caused by intermittent biliary obstruction. When determinations of SGOT and SGPT were made in patients with gastro-intestinal diseases, normal results were obtained. Transaminase determinations proved of value in prognosis because they permitted an evaluation of the severity of liver damage to be made in hepatitis and cirrhosis. Persistently elevated levels following hepatitis indicated residual complications and delayed recovery. Rising levels in cases of liver metastases indicated a poor prognosis.

THE DIAGNOSIS OF CANCER OF THE PANCREAS, BILIARY TRACT, AND DUODENUM BY COMBINED CYTOLOGIC AND SECRETORY METHODS. I. EXFOLIATIVE CYTOLOGY AND A DESCRIPTION OF A RAPID METHOD OF DUODENAL INTUBATION.

Raskin, H. F.: Wenger, J.; Sklar, M.; Pleticka, S., and Yarema, W. *Gastroenterology* **34:** 996 (June) 1958.

A method of duodenal intubation is described which is rapid (fifteen minutes), reliable, and well tolerated, and which requires a minimum of fluoroscopic exposure. A double-lumen

radiopaque tube (the Diamond tube) has proved most satisfactory. After proper positioning of the tube, the duodenal content and the acid gastric secretion are aspirated separately and the latter discarded. When adequate gastric drainage and proper duodenal drainage have been secured, a control sample of the duodenal content is collected and saved. Then a dose of 1 unit of secretin per kilogram of body weight is injected intravenously and the pancreatic secretion collected for half an hour in three 10-minute samples in order to determine the maximum pancreatic response. The duodenal aspirate is centrifuged and the sediment fixed on slides for cytologic examination. Malignant cells, when found in the aspirate, are characterized by variations in size and shape (in contrast to normal duodenal epithelial cells), vacuolated cytoplasm, heavy chromatin clumping within the nucleus and occasional eosinophilic nucleoli. There usually are few cells and they are likely to occur in groups of two or three rather than in clumps. It may not be possible to tell whether the cells come from the pancreas or the biliary system, but a squamoid appearance suggests origin in the biliary ducts. The combined cytologic and chemical analysis of pancreatic secretion and duodenal content has been in use for approximately two years. During this time malignant cells were recovered from 28 (65 per cent) of 43 patients subsequently proved to have carcinoma of the pancreas, biliary tract, gallbladder, or duodenum. The patients in whom no malignant cells were found have been observed for a sufficiently long time for carcinoma of the pancreas to have been confirmed by conventional methods if it had been present. Six case reports illustrate the use of the cytologic method. Exfoliative cytologic study of the pancreas and biliary tract is improved by the use of secretin to stimulate pancreatic secretion. Malignant cells will not, however, be recovered in cases in which there is obstruction of the pancreatic or biliary ducts. The finding of malignant cells will not guarantee that the surgeon will be able to locate the carcinoma that is their source. The exfoliative cytology technic appears to offer some possibility of making an early diagnosis in pancreatic carcinoma.

GRAVITATIONAL LEG ULCERS IN THE ELDERLY.

Rivlin, S. *Lancet* **1:** 1363 (June 28) 1958.

A study was made of 200 cases of gravitational ulceration, 93 instances of which were in persons above 60 years of age. Seventy-five per cent were varicose, 15 per cent post-thrombic, and 10 per cent from miscellaneous causes. Rivlin previously has shown that varicose veins produce edema by an alteration in tissue-fluid hydrostatics due to an increase in average venular pressure. Deep venous thrombosis does the same thing. Ulcers also arise in limbs with edema which is due to the failure of weakened or poorly used calf muscles to maintain an adequate venous return, as in hemiplegia, rheumatoid arthritis, and arthritis of the hip and knee. A complete history and examination of the patient are essential to accurate diagnosis and classification of the type of ulcer. Treatment of gravitational ulcers is aimed at abolishing the edema, and healing. Most important is ambulation and the wearing of laced shoes. For patients who cannot walk, the simplest method of treatment is to tip the bed so that the legs are higher than the heart, but this is not desirable in elderly patients. Bandaging speeds healing by taking up the slack left by the vanishing edema. A paste underbandage is applied first in order to lessen irritation and because such ingredients as zinc, ichthammol, urethane, and calomine assist healing. This is covered with a flexible (not elastic) adhesive bandage which does not loosen as it is worn. Application of the bandages requires a precise technic that is described. The first bandage remains in place for a week and then continuation bandages are applied until the ulcer has healed. Healing of gravitational ulcers in elderly persons, once edema was overcome, was found to take place as rapidly as in younger persons. The elderly patients were under treatment longer, however, because the ulcers originally were larger in size. Varicose ulcers were found to heal faster than the other types. Varicose ulcers can be cured by operation on the veins once the ulcer has healed. Post-thrombotic and miscellaneous ulcers can be healed, but the prevention of recurrence of edema will require that the patient follow the practice of walking, of wearing laced shoes, of sleeping with the foot of the bed raised nine inches, and of wearing an elastic support on his legs. A new light-weight all-way-stretch supporting bandage is used for this purpose.

SERUM GLUTAMIC OXALOACETIC TRANSAMINASE IN DISSECTING ANEURYSM OF THE THORACIC AORTA.

Tredway, J. B., and Kemble, E. E. *Circulation* **18:** 37 (July) 1958.

Determination of the serum glutamic oxaloacetic transaminase level is not a reliable guide to separating the diagnoses of myocardial infarction and dissecting aortic aneurysm. In 2 of 3 cases of the latter, the patient had an elevated serum level of this enzyme. This was associated with an extension of the dissection into the pericardial sac. The possibility is considered that the hemolyzed dissecting blood may have given rise to an elevated level in the serum but this is probably not the sole cause, since gross hemolysis of the serum was not present. A second possibility is that the elevated levels resulted from the presence of blood in the pericardial sac, but the true mechanism remains to be determined.

THE DIAGNOSIS OF CANCER OF THE PANCREAS, BILIARY TRACT, AND DUODENUM BY COMBINED CYTOLOGIC AND SECRETORY METHODS. II. THE SECRETIN TEST.

Wenger, J., and Raskin, H. F. *Gastroenterology* **34:** 1009 (June) 1958.

Using the secretin test for pancreatic function and the cytologic examination of duodenal fluid (Raskin *et al.*, 1958) in combination may facilitate the diagnosis of carcinoma of the pancreas, biliary system, and duodenum. In normal persons without pancreatic disease, the volume of duodenal fluid aspirated by the Diamond tube (as described by Raskin) exceeds 1.1 ml. per Kg. in the 30-minute collection period following stimulation by the injection of secretin. The bicarbonate concentration of the fluid normally is 90 mEq. or greater in at least one of three 10-minute collections of pancreatic secretion. The analysis for pancreatic enzymes adds nothing in the diagnosis of pancreatic malignancy and the technic is simplified by omission of this determination. The result of the secretin test must be interpreted cautiously, since borderline or abnormal responses may be observed in such diseases as chronic diffuse pancreatitis, diabetes mellitus, cirrhosis, and hemochromatosis. The secretin test appears to be most sensitive in the case of tumors of the head and body of the pancreas. In 32 proved cases of carcinoma of the pancreas, secretin tests indicated abnormal pancreatic function in 24 (75 per cent). Among 35 cases of cancer of the pancreas, either the secretin test or exfoliative cytologic examination suggested the diagnosis in 31 patients (88.6 per cent). Among 5 cases of cancer of the bile ducts, 1 of carcinoma of the gallbladder, and 3 of duodenal carcinoma, cytologic examination correctly diagnosed the condition in 7 instances and was somewhat more helpful diagnostically than the response to secretin. This test was less useful because of impairment of pancreatic function in 1 patient with a ductal tumor and in 2 with metastatic malignancy of the duodenum, because of obstruction to passage of the tube. The over-all accuracy of the combined methods was 38 correct diagnoses in 44 cases, or 86 per cent.

THE ROLE OF THE KIDNEY IN THE PATHOGENESIS AND TREATMENT OF GOUT.

Wyngaarden, J. B. *Arthritis & Rheumatism* **1:** 191 (June) 1958.

Present evidence suggests that the hyperuricemia of gout is caused by overproduction of uric acid, and that the renal mechanisms for handling urate are essentially normal in the gouty individual. However, renal disease develops as a concomitant, or consequence, of the disease in a high percentage of patients. Renal insufficiency is a particularly serious matter for the gouty individual, for accumulation of urate is then apt to occur at an accelerated pace. Although renal disease remains an important cause of death in gout, patients may tolerate minor degrees of renal involvement for many years. Accelerated nephrosclerosis is the common renal lesion, but gout nephrosis, involving renal urate deposits, is found in the kidneys of most gouty patients, though rarely in severe form. The development of gouty renal disease in the absence of articular gout is probably more common than is generally recognized. The treatment of gout includes in most patients the use of drugs which promote renal excretion of uric acid by suppressing tubular reabsorption. Whether the use of such drugs will reduce the incidence or severity of renal complications of gout remains to be determined. (From author's summary.)

BOOKS RECEIVED

Receipt of the following books for review is hereby acknowledged. We are glad to publish complete listings of all new books received but such listing must be regarded as a sufficient return for the courtesy of the sender. Books of particular interest will be reviewed in full as time and space permit. Additional information in regard to all listed books will be gladly furnished upon request.

HORMONE PRODUCTION IN ENDOCRINE TUMOURS—Ciba Foundation Colloquia on Endocrinology, Volume XII. Edited by *G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Maeve O'Connor, B.A.* Cloth. $9.00. Pp. 295. 58 Illustrations and Cumulative Index to Volumes 1–12. J. & A. Churchill Ltd., London, and Little, Brown and Company, Boston, Massachusetts, 1958.

WATER AND ELECTROLYTE METABOLISM IN RELATION TO AGE AND SEX—Ciba Foundation Colloquia on Ageing, Volume 4. Edited by *G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Cecilia M. O'Connor, B.Sc.* Cloth. $8.50. Pp. 327. 85 Illustrations. J. & A. Churchill Ltd., London, and Little, Brown and Company, Boston, Massachusetts, 1958.

THE CEREBROSPINAL FLUID—Ciba Foundation Symposium. Edited by *G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Cecilia M. O'Connor, B.Sc.* Cloth. $9.00. Pp. 335. 141 Illustrations. J. & A. Churchill Ltd., London, and Little, Brown and Company, Boston, Massachusetts, 1958.

NEUROLOGICAL BASIS OF BEHAVIOUR—Ciba Foundation Symposium. Edited by *G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Cecilia M. O'Connor, B.Sc.* Cloth. $9.00. Pp. 400. 109 Illustrations. J. & A. Churchill Ltd., London, and Little, Brown and Company, Boston, Massachusetts, 1958.

PHYSICAL DIAGNOSIS—Fourteenth Edition. By *F. Dennette Adams, M.D.*, Physician, Board of Consultation, Massachusetts General Hospital; Consultant to The Surgeon General, U. S. Army; Consultant to Boston and Bedford, Mass. Veterans Administration Hospitals; formerly Assistant Clinical Professor of Medicine, Harvard Medical School. Cloth. $12.00. Pp. 926. The Williams & Wilkins Co., Baltimore, Maryland, 1958.

THE PRINCIPLES AND PRACTICE OF MEDICINE. A Textbook for Students and Doctors—Fourth Edition. By *Sir Stanley Davidson, B.A. Cantab., M.D., F.R.C.P.Ed., F.R.C.P.Lond., M.D.Oslo*, Physician to H.M. the Queen in Scotland; Professor of Medicine and Clinical Medicine, University of Edinburgh; Physician-in-Charge, Royal Infirmary, Edinburgh, and The Staff of the Department of Medicine, University of Edinburgh, and Associated Clinical Units. Cloth. $8.00. Pp. 1067. E. & S. Livingstone Ltd., Edinburgh, 1958. The Williams & Wilkins Co., Baltimore, exclusive U. S. agents.

BASIC CARDIOLOGY. By *T. E. Gumpert, M.B., Ch.B. (Sheff.), F.R.C.P. (Lond.)*, Physician Royal Hospital, Sheffield, and Jessup Hospital for Women, Sheffield; Lecturer in Medicine, University of Sheffield; Examiner in Medicine to the Conjoint Board of England. Cloth. $6.00. Pp. 168. John Wright and Sons Ltd., Bristol, 1958. The Williams & Wilkins Co., Baltimore, exclusive U. S. agents.

PATHOPHYSIOLOGY IN SURGERY. By *James D. Hardy, M.S. (Chem.) M.D., F.A.C.S.*, Professor and Chairman, Department of Surgery, and Director of Surgical Research, University of Mississippi Medical Center; Surgeon-in-Chief, Hospital of the University of Mississippi; Chief Surgical Consultant, Jackson Veterans Hospital and Mississippi Tuberculosis Sanatorium. Cloth. $19.00. Pp. 704. The Williams & Wilkins Company, Baltimore, Maryland, 1958.

A CLASSIFIED BIBLIOGRAPHY OF GERONTOLOGY AND GERIATRICS. Supplement One, 1949–1955. By *Nathan W. Shock*, Chief, Gerontology Branch, National Heart Institute, National Institutes of Health, and the Baltimore City Hospitals. Cloth. $15.00. Pp. 525. Stanford University Press, Stanford, California, 1957.

A DOCTOR SPEAKS HIS MIND. By *Roger I. Lee, M.D.* Cloth. $3.00. Pp. 120. Little, Brown & Company, Boston, Massachusetts, 1958.

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